Treatment of Anorexia Nervosa: Translating Experimental Neuroscience into Clinical Practice

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General abstract

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Objectives

Anorexia nervosa (AN) is a severe psychiatric condition and evidence on how to best treat it is limited. This programme consists of seven integrated work packages (WP) and aims to develop and test targeted, disseminable and cost-effective treatments to optimise management for people with AN across all stages of illness.

Methods

WP1a used surveys, focus groups and a pre-post trial to develop and evaluate a training programme for school staff on eating disorders (ED). **WP1b** used a cluster randomised controlled trial (RCT, ISRCTN42594993) to evaluate the efficacy of a teacher-delivered prevention programme for ED in schools. **WP2a** evaluated an inpatient treatment for AN using case reports, interviews and a quasi-experimental trial. **WP2b** used an RCT (ISRCTN67720902) to evaluate two outpatient psychological therapies for adults with AN. **WP3** used an RCT (ISRCTN06149665) to evaluate an intervention for carers of inpatients with AN. **WP4** used actimetry, self-report and endocrine assessment to examine physical activity in AN. **WP5** conducted a feasibility RCT (ISRCTN18274621) of an email-guided relapse prevention programme for inpatients with AN. **WP6** analysed cohort data to examine the effects of maternal ED on fertility and their children's diet and growth. **WP7a** examined clinical casenotes to explore how access to specialist ED services effects care pathways and user experiences. Finally, **WP7b** used data from this programme and the British Cohort Study to identify the costs of services used by people with AN and to estimate the annual costs of AN for England.

Key findings

- **WP1a:** A one day training programme improved self-reported knowledge, attitudes and confidence of schools staff in identifying and managing ED in school.
- **WP1b**: A teacher-delivered intervention was feasible and improved risk factors for ED in adolescent girls.
- **WP2a:** Both psychological therapies improved outcomes in outpatients with AN similarly, but patients preferred one of the treatments.

- **WP2b:** The inpatient treatment CREST was acceptable with perceived benefits by patients, but showed no benefits compared to treatment as usual (TAU).

- **WP3:** Compared to TAU, the carer intervention improved a range of patient and carer outcomes, including carer burden and patient ED symptomatology.

- **WP4**: Drive to exercise is tied to ED pathology and a desire to improve mood in AN patients. In contrast, actual activity levels are unrelated to ED pathology.

- **WP5:** Compared to TAU, the email-guided relapse prevention programme resulted in higher BMI and lower distress in patients at 12 months discharge.

- **WP6:** Women with ED had impaired fertility and their children had altered dietary and growth patterns compared to the children of women without ED.

- **WP7a:** Direct access to specialist ED services was associated with higher referral rates, lower admission rates, greater consistency of care and greater user satisfaction.

- **WP7b:** The annual costs of AN in England are estimated at between £45m and £230m for 2011.

Conclusions

This programme has produced evidence to inform future intervention development and has developed interventions that can be tested further or disseminated to improve outcomes for individuals with AN.

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List of abbreviations

AESED	Accommodation and Enabling Scale for Eating Disorders
AN	Anorexia Nervosa
ANX	Anxiety
ARIADNE	Applied Research into Anorexia Nervosa and Not Otherwise Specified Eating Disorders
BCS-70	British Cohort Study (1970)
BMC	Bone Mineral Content
BMI	Body Mass Index
BN	Bulimia Nervosa
CAB	Citizen's Advice Bureau
CAMHS	Child and Adolescent Mental Health Service
CBT	Cognitive Behavioural Therapy
CES	Commitment to Exercise Scale
CIA	Clinical Impairment Assessment
CPN	Community Psychiatric Nurse
CREST	Cognitive Remediation and Emotional Skills Training
CSO	Clinical Studies Officer
CSRI	Client Services Receipt Inventory
CTU	Clinical Trials Unit
DASS	Depression, Anxiety and Stress Scale
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition
DWP	Department for Work and Pensions
EAI	Exercise Addiction Inventory
ECHO	Experienced Carers Helping Others
ED	Eating Disorders
EDE-Q	Eating Disorder Examination – Questionnaire
EDNOS	Eating Disorder Not Otherwise Specified
EDSIS	Eating Disorder Symptom Impact Scale
FPT	Fragmented Pictures Task

FQ	Family Questionnaire
GAD	Generalized Anxiety Disorder
GDTE	General Drive to Exercise
GEE	Generalised Estimating Equations
GEFT	Group Embedded Figures Task
GP	General Practitioner
HC	Healthy Control
ICC	Intra-Cluster Correlation
IFT	Individual Family Therapy
iMANTRA	Internet based MANTRA
IP	Inpatient
IPAQ	International Physical Activity Questionnaire
IQ	Intelligence Quotient
ITT	Intention to treat analysis
IUS	Intolerance of Uncertainty Scale
MANTRA	Maudsley Model of Treatment for Adults with Anorexia Nervosa
MAR	Missing At Random
MFDT	Multiple-Family Day Treatment
MFT	Multi-Family Therapy
MHRN	Mental Health Research Network
MOSAIC	Maudsley Outpatient Study of Treatments for Anorexia Nervosa and Related conditions
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NS-NS	Non-specialist – Non-specialist care pathway
NS-S	Non-specialist – Specialist care pathway
OCD	Obsessive Compulsive Disorder
OCI-R	Obsessive Compulsive Inventory Revised
OEQ	Obligatory Exercise Questionnaire
OP	Outpatient
OR	Odds Ratio

PA	Physical Activity
PCT	Primary Care Trust
PDT	Psychodynamic Psychotherapy
PI	Ponderal Index
PPI	Patient and Public Involvement
PSWQ	Penn State Worry Questionnaire
RCP	Royal College of Psychiatrists
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
REI	Reasons for Exercise Inventory
REY	Rey-Osterrieth Complex Figure Test
RME	Reading the Mind in the Eyes Task
RMF	Reading the Mind in the Eyes Task
SCID	Structured Clinical Interview for DSM
SEED	Short Eating Disorders Symptom Scale
S-S	Specialist – Specialist care pathway
SSCM	Specialist Supportive Clinical Management
TAU	Treatment As Usual
VAS	Visual Analogue Scale
WCST	Wisconsin Card Sorting Task
WHO	World Health Organization
WHOQOL-100	World Health Organisation Quality of Life Questionnaire
WP	Work Package
YPLL	Years of Potential Life Lost

Scientific summary

Background

Anorexia nervosa (AN) is characterised by self-starvation, weight loss, hyperactivity, and in some cases bingeing and purging. Psychological features include morbid fear of fatness and body image disturbance. Neuro- and social-cognitive impairments may contribute to onset and maintenance of the illness. Physical complications affect all organs. The risk of death or disability is high. Quality of life is poor. The family are usually the main carers, and they experience significant distress in this role. Those who become pregnant have high risk pregnancies and have difficulties feeding and playing with their children. Many parts of the UK lack NHS provision of specialist services for AN. There is therefore a need to develop better treatments and disseminate specialist interventions.

Aims & Objectives

The overall aim of this programme was to improve knowledge of optimal disease management for people with AN at all stages of illness. To achieve this, seven work packages (WP) had the following objectives:

1a. To develop a training programme for school staff to enable them to detect and manage eating disorders (ED).

1b. To develop and test a schools-based prevention programme for risk factors of ED.

2a. To develop an improved outpatient treatment for adults with AN and to evaluate the efficacy, cost and cost-effectiveness of this treatment.

2b. To test components of this treatment, designed as intensive modules for inpatients with AN

3.   To evaluate the efficacy, cost and cost-effectiveness of a carer skills training intervention.

4.   To produce improved understanding of the nature of a debilitating core symptom of AN, i.e. hyperactivity.

5.   To develop and test a relapse prevention programme for in-patients with AN.

6.   To obtain information on the needs of mothers with ED and the risks for their offspring to inform the development of an intervention for mothers with ED.

7a. To study existing care pathways for AN, with a focus on the impact of having access to specialist eating disorder services.

7b. To study service utilisation and cost of illness in ED.

Work Package 1a: Detection and early intervention

This WP designed and evaluated a teacher training programme to improve school staff's knowledge and attitudes about ED and their confidence to manage ED in school. Studies one and two explored the experiences of ED in 511 secondary school students and 826 school staff using online questionnaires. Only 7% of students would confide in a teacher about an ED. 74% of staff had received no training on ED. In study three, 63 members of staff from 29 UK schools participated in focus groups asking them about their training needs in relation to early detection and management of ED. In study four, 45 school staff participated in a one day ED training programme based on the earlier findings. Participants completed a questionnaire about their ED knowledge, attitude and confidence at pre-intervention, post-intervention and three months follow up. The intervention had a significant positive impact on these outcomes, with gains maintained at three months.

Work Package 1b: Prevention

This WP aimed to design and evaluate a universal prevention programme for ED in secondary schools. The intervention consisted of six sessions, delivered by teachers targeting risk factors for ED and was evaluated using a cluster randomised controlled trial (RCT) comparing intervention lessons to a curriculum-as-usual control in 448 female school students. Participants completed questionnaire measures at pre-intervention, post-intervention and three month follow-up. There were significant between group differences in body esteem favouring the intervention group at post-intervention ($d = 0.12$) and three month follow-up ($d = 0.19$). There were also significant between group differences in thin-ideal internalization ($d = 0.17$, maintained at follow-up, $d = 0.16$), and self-esteem ($d = 0.20$, not maintained at follow-up). There were no between group differences for the other outcomes. Fidelity to intervention material and acceptability of the programme varied across the three schools.

Work Package 2a: Outpatient treatment

This WP evaluated the efficacy of a novel psychological therapy for AN (Maudsley Model of Anorexia Nervosa Treatment for Adults, MANTRA) compared with specialist supportive clinical management (SSCM) in a multi-centre RCT. Participants were adult outpatients,

meeting DSM-IV criteria for AN or AN-type eating disorder not otherwise specified (EDNOS-AN), recruited from four specialist ED services in England. Participants were randomised to 20 once weekly sessions of MANTRA or SSCM and optional additional sessions depending on severity and clinical need. 72 patients were allocated to MANTRA and 70 were allocated to SSCM. Patients in both treatments improved significantly in terms of BMI, eating disorder and other outcomes, with no differences between groups. Patients rated MANTRA as more acceptable and credible than SSCM at 12 months. As such, both treatments appear to have value as first line outpatient treatments of adults with AN.

Work Package 2b: Inpatient treatment

This WP aimed to evaluate Cognitive Remediation and Emotional Skills Training (CREST) for inpatients with AN. CREST is an intervention teaching cognitive, emotion regulation, recognition and processing skills. The evaluation involved a qualitative study of service users' views about CREST and a quasi-experimental comparison of CREST plus treatment as usual (TAU) versus TAU alone in two inpatient settings. The qualitative assessments demonstrated CREST to be acceptable to patients. However, the quantitative data showed no difference between CREST and TAU groups in neuropsychological or clinical outcomes. Future work will focus on revisions to the CREST manual.

Work Package 3: Carer interventions

This WP aimed to examine the impact of the addition of ECHO, a skills-training programme for carers, to standard inpatient care. Patients with AN and their carers were recruited from 15 inpatient services in the UK. Patients were randomly allocated to either receive ECHO (a book, DVDs and 10 telephone coaching sessions) added to TAU or TAU only. 178 families were recruited and patient and carer outcomes were measured at discharge and 6 and 12 months after discharge. Compared to TAU only patients, patients in the ECHO group had significantly reduced ED psychopathology and improved quality of life at 6 months. Carers in the ECHO group spent less time caregiving, had lower carer burden and lower levels of unhelpful caregiving behaviour at 6 months compared to carers on the TAU only group. Sharing skills and information with family members is therefore of benefit for patients and carers.

Work Package 4: Activity in AN

This WP aimed to explore physical activity (PA) in AN and associations between drive to exercise, ED pathology, anxiety and endocrine measures. Female participants were recruited into four groups: AN-outpatients ($n = 37$), AN-inpatients ($n = 18$), an anxiety group ($n = 34$) and healthy controls ($n = 30$). Actigraphy and self-report were used to measure PA, together with drive/reasons for exercise, ED psychopathology, depression, anxiety, stress, BMI, body composition, salivary cortisol and serum leptin levels. Psychopathology and endocrine measures were consistent with diagnosis. Levels of (especially self-reported) PA were highly variable. Objective PA levels did not differ significantly between groups, yet AN groups reported 57-92% higher total PA than HCs. Drive to exercise was significantly higher in AN groups, who rated 'improving tone' and affect regulation as important and health and enjoyment as less important exercise motivators.

Work Package 5: Relapse prevention

This WP aimed to assess the feasibility of a relapse prevention programme and to acquire information to inform a future RCT. Participants ($n = 41$) were inpatients with AN who were randomly allocated at discharge from hospital to receive a manual-based e-mail guided self-care intervention (iMANTRA, see WP2a) for twelve months combined with TAU or TAU alone. Outcome assessments included BMI, ED and general psychopathology, quality of life and service utilisation. At 6 months post-randomisation there was little difference between groups. At 12 months, patients receiving the experimental intervention had a higher BMI ($d = 0.41$) and lower scores on the Depression, Anxiety and Stress Scale ($d = 0.64$). Readmission rates were 5/22 (22.7%) in the experimental group and 5/16 (31.2%) in the TAU group. These findings suggest that this low-intensity relapse prevention intervention has potential in the aftercare of inpatients with AN and that a large-scale RCT is justified.

Work Package 6: Mothers with ED

This WP consisted of three studies examining the effects of maternal ED on fertility, their offspring's diet and growth. Participants were 11,088 women from the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort and their children. The outcome measures were maternal report of fertility difficulties, maternal report of child diet (up to 103 months), and child weight and height (up to age 10 years). Women with ED reported more fertility difficulties. There was a complex pattern of differences in diet, trajectories of height, ponderal index and body mass index in children of women with ED to compared to those

without ED. These results suggest that continuity of care from pre-conception to the post-natal period is paramount for women with ED.

Work Package 7a: Service utilisation

This WP aimed to explore how access to specialist outpatient eating disorders services affects rates of referrals, admissions for inpatient treatment, continuity of care, and service user experiences. Mental health services in London were asked to identify adolescents who presented for treatment of an ED over a period of two years. Retrospective data about service use was collected from casenotes. A small sample of adolescents and parents were interviewed about their experiences of services. Direct access to specialist outpatient services was associated with higher referral rates, lower admission rates, and greater consistency of care. Service users identified a number of advantages of specialist service provision. This suggests that facilitating direct access to specialist services for adolescents with AN may result in better outcomes, lower costs, and higher satisfaction among service users.

Work Package 7b: Economic evaluation

This WP aimed to identify services and treatments used by people with AN and associated costs, estimate unit costs of ED treatments, explore cost variations by patient characteristics, explore the economic consequences of AN and estimate the annual costs of AN for England. Data collected in WPs 2a, 3 and 7a and from the British Cohort Study were used. Service costs were driven by hospital admissions, costs vary based on age, ethnicity, severity of illness and treatment history. Those treated in non-specialist outpatient services incurred higher costs than those treated in specialist services only, but there were no differences in outcome. Women with AN were more likely to be long-term sick or disabled in adulthood, receive benefits and have completed a degree, with no differences in weekly income or employment compared to people without AN. The annual costs of AN in England are estimated at between £45m and £230m.

Overall conclusions

This programme has focused on development of interventions for AN and related ED. The programme's studies have a number of important implications for the management of AN (and ED) across the full course of this disorder. Future research is essential to further our understanding of optimal disease management for AN.

Recommendations for healthcare

- Brief training can improve school staff knowledge and attitudes towards ED. Staff can also be trained to delivered efficacious preventative interventions. Following effectiveness testing, these interventions may improve management and prevention of ED in schools.

- In adult outpatients with AN both MANTRA and SSCM significantly improve clinical outcomes, but patients see MANTRA as more acceptable and credible. Both interventions can be considered as first-line outpatient treatments.

- In adult inpatients with AN, CREST is valued by patients, but the addition of CREST to TAU is not is not superior to TAU alone. Further work is needed to determine CREST's role in inpatient care.

- The addition of an intervention for carers of people with AN to inpatient treatment reduces carer time caregiving, burden and unhelpful caregiving behaviours. Patients show reduced ED psychopathology and improved quality of life. Skills sharing with family members benefits patients and carers.

- Exercise is driven and rewarding to sufferers with AN. Clinicians need to develop interventions that address the pathological drive to exercise rather than exercise per se.

- iMANTRA is a feasible and safe intervention, which has promise in the aftercare of inpatients with AN.

- ED are common in pregnancy and they are associated with unplanned pregnancies and fertility treatment. Children of mothers with ED are at risk of growth difficulties and disordered eating patterns. Interventions for mothers with ED may benefit them and their children.

- There are clear benefits in having specialist community based outpatient services which are easily accessible from primary care: they provide good clinical outcomes with significantly lower rates of hospital admissions and better continuity of care than generic services can deliver.

- AN is associated with a high risk of adult disability. Effective prevention and early intervention to prevent long-term disability are therefore likely to provide patient benefit and cost savings. While inpatient treatment is the largest contributor to treatment costs, participants with AN access a wide range of services. There may be

scope to develop collaborations with community-based services to improve early identification and ensure appropriate treatment.

Recommendations for research

- To carry out a fully powered study to test the effectiveness of the school staff training programme developed in WP1a.
- To conduct a large scale cluster RCT of the prevention programme developed in WP1b to determine effectiveness of this programme in a range of school environments.
- To gain two year follow up data from the RCT in WP2a, which are essential to determine the relative efficacy of the two psychological treatments and the maintenance of treatment gains.
- To conduct an RCT to explore benefits of CREST (examined in WP2b) in comparison to other manualised treatments of similar length.
- To examine whether adding the carer intervention evaluated in WP3 onto standard outpatient care improves outcomes and to examine whether adding a more intensive family intervention (workshops) improves inpatient care.
- To replicate findings in a larger sample and to develop and test interventions targeting drive to exercise in AN.
- To carry out a large scale RCT of iMANTRA (piloted in WP5), with economic analyses, and longer term follow ups.
- To follow the children and women with ED into adolescence and develop and test a tailored intervention for pregnant women with ED.
- To evaluate the role of specialist ED services beyond the metropolitan London context in a larger scale study.
- To conduct a longitudinal study investigating the impact of AN on education, employment and potential earnings differential and to use longer-term follow-ups of clinical trials with accompanying economic evaluation to better reflect the longer-term costs of treatment.

Study registrations

The RCTs are registered as follows: **WP1b:** ISRCTN42594993, **WP2a:** ISRCTN67720902, **WP3:** ISRCTN06149665, **WP5:** ISRCTN18274621.

Plain English summary

Word count: 250 (max 250)

Anorexia nervosa (AN) is an eating disorder (ED) with serious consequences for sufferers and their families. We do not currently know how best to treat people with anorexia nervosa, especially those with a severe illness. We carried out ten studies to improve our understanding.

We evaluated six interventions:

- teacher training on managing ED
- school lessons aiming to prevent ED
- an outpatient talking therapy for adults
- an inpatient treatment for adults
- an intervention for carers of people with AN
- an online intervention to prevent relapse after treatment

We also studied two things that will help us to develop better treatments in the future:

- the levels of physical activity in people with AN
- fertility problems in women with ED and the growth and diet of their children

And, finally, we studied:

- the importance of specialist services in treating ED
- the cost of treatments for AN and the total costs of AN in England each year

We found that:

- participants liked the new interventions
- most of the interventions were more helpful than treatment as usual
- the new outpatient treatment was as helpful as an established gold-standard treatment and better liked
- people with ED were different to healthy individuals in some aspects of their physical activity, their fertility, and the growth and diet of their children
- having access to specialist services meant that patients had more positive experiences
- AN costs between £45m and £230m in England each year.

Overall, these studies have greatly improved our understanding of how best to help

individuals with AN.

Chapter 1. Background and structure of the report

Helen Sharpe, Susan Ringwood & Ulrike Schmidt

Introduction

Anorexia nervosa (AN) has existed throughout different epochs and cultures (1). Key symptoms are restricted food intake, weight loss, hyperactivity, and in some cases bingeing and purging. Psychological features include morbid fear of fatness and body image disturbance. AN typically affects young females, although it also affects some men (2). AN usually starts in adolescence, when brain development is incomplete (3). Starvation can impair brain function in a lasting way (4). Early intervention is essential in producing good outcomes (5). Treatments in the later stages of illness are much less successful. AN is highly heritable but environmental factors are aetiologically important (6, 7). Progress has been made in identifying risk factors for AN (e.g. premorbid feeding problems, obsessive compulsive and anxious traits, high levels of exercising and overinvolved parenting) (6, 7). Research on the genetic, epigenetic and neurobiological underpinnings of eating disorder (ED) psychopathology (8-13) has identified neuro- and social-cognitive biomarkers, such as impaired set-shifting, poor central coherence or emotion processing impairments, including poor theory of mind (14-18), which have the potential to inform predictions of treatment outcome and prognosis. A key challenge is to utilise all this knowledge to develop targeted treatments. To this end, we have developed a model of how AN arises and is maintained, informed by these and other clinical neuroscience findings and with the aim of guiding treatment (19, 20).

People with AN consult their GP significantly more than others in the 5 years prior to diagnosis (21). A single consultation about eating or weight/shape concerns strongly predicts the subsequent emergence of AN (22). Although GPs exclusively treat 20% of cases with AN (23), they are often not confident at managing AN (24), and there is usually a considerable delay between a diagnosis being made in primary care and the point where more specialist help becomes available (25).

Many parts of the UK lack NHS provision of specialist services for AN (26, 27). Treatment by non-specialists is problematic as many patients are admitted unnecessarily and for lengthy periods (28), with extra costs to the NHS (29). For example, 35% of people with AN seen in non-specialist Child and Adolescent Mental Health Services are admitted to hospital, contrasting with only 10% of those seen in specialist ED services (30). More child and adolescent psychiatric beds (20%) are occupied by young people with AN than any other diagnostic group (31). Weight gain (32) and longer-term outcomes (33) are poor in non-

specialist units and the mortality is higher (34, 35). Thus, there is a need to disseminate specialist knowledge of this illness. Transitions between services (e.g. from child to adult services; home to university health services; inpatient to follow-up care) are common and can result in fragmented care, thus putting patients at risk (36, 37).

Life-time prevalence rates for AN are 1.6% in women and 0.3% in men (7). The median duration of illness is 6 years (38). Physical complications affect all organs (39) and the risk of death is the highest of any psychiatric disorder (40). Those who become pregnant, have high risk pregnancies and difficulties feeding and playing with their children (41). Severe psychiatric comorbidity is common (42). Quality of life is severely impaired (43), more than in depression (44). The cost-per case of AN is at least that of schizophrenia (45, 46). AN has the highest proportion of admissions with a length of stay over 90 days (26.8%) and the longest median length of stay (36 days) (28). Eating disorders are one of the leading causes of disease burden in terms of years of life lost through death or disability in young women (47). The family are usually the main carers. They report similar difficulties to carers of people with psychosis, but are more distressed (25, 48). The burden of caregiving and other societal costs have never been examined in economic terms.

This report presents the results of seven independent but integrated work packages (WP), which form the ARIADNE programme (Applied Research into Anorexia Nervosa and Not Otherwise Specified Eating Disorders). These WPs focus on optimal disease management for people with AN at all stages of illness, from prevention and detection through to treatment and preventing relapse. The studies focus on a range of populations, including samples from the community, those drawn from inpatient and outpatient settings, as well as specialist groups, such as mothers with eating disorders (ED) and carers of those with ED. The majority of our WPs focus on building evidence on the efficacy and effectiveness of interventions for these populations, grounded in our clinical neuroscience model of AN. We report on findings from six independent interventions that have been developed and tested by the ARIADNE group during this programme. In addition, we present analyses of the economic and clinical implications of existing care pathways and patterns of service use.

Aims and objectives of the ARIADNE Programme

Broad aims

Responding to the need for high quality research into the management of AN, the overarching aims of the ARIADNE programme were:

1. To produce, validate and disseminate improved evidence-based interventions for AN.

2. To collaborate with patients and carers throughout the project.

3. To improve clinical outcomes in AN, by early detection and intervention, by reducing chronicity and relapse, and by improving carer outcomes.

4. To improve acceptability and cost-effectiveness of AN treatments.

5. To deliver standardised, trainable and disseminable AN treatments.

6. To assess service utilisation and NHS costs of AN and implications of changes in clinical practice for patient care and resources.

Objectives

Our objectives were:

1a. To develop a training programme for school staff to enable them to detect and manage eating disorders.

1b. To develop and test a schools-based prevention programme for risk factors for ED.

2a. To develop an improved treatment for adults with AN that targets disease-maintaining factors, is matched to symptoms, personality and neuropsychological profile and which can be used as a first-line treatment in out-patient settings. To evaluate the efficacy, cost and cost-effectiveness of this treatment.

2b. To test and validate components of this treatment, designed as intensive modules for inpatients with AN (i.e. those with severe, chronic or treatment-resistant AN)

3. To evaluate the efficacy, cost and cost-effectiveness of a carer skills training intervention, and to assess its impact on carer outcomes (e.g. distress, care giving efficacy) and patient outcomes.

4. To improve understanding of the nature of a debilitating core symptom of AN, i.e. hyperactivity.

5. To develop and test a relapse prevention programme for inpatients with AN.

6. To obtain information on the needs of mothers of children with eating disorders and the risks of the maternal ED for their off-spring and to use this information to inform the development of an intervention for mothers with ED to minimise the impact of their ED on their children.

7a. To study existing care pathways for AN, with a focus on the impact of having access to specialist ED services.

7b. To study service utilisation and cost of illness in ED.

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Patient and public involvement in the ARIADNE Programme

Patient, carer and public involvement (PPI) has been central to the research in the ARIADNE Programme. Mrs Susan Ringwood, the Chief Executive Officer of Beat (the main UK patient carer organisation for eating disorders) was a co-applicant on the Programme. As such, she was involved in the development of the overall programme aims, ensuring that the research questions were aligned with patients' and carers' needs. Patients are carers were also part of the programme steering group.

Examples of PPI in specific WPs are:

Example 1: Early intervention in schools

WP1a involved the development and pilot testing of a teacher training programme for ED (see *Chapter 2*). This research was devised and led by a former ED service user. It involved an extensive period of public consultation, which was used to assess the needs of both school staff and school students in this area. Thorough consultation was achieved through online surveys reaching over 800 school staff and over 500 students. Intervention materials for the training programme were then developed using an iterative process in which two panels of school staff (six members per panel) reviewed draft materials and their feedback was incorporated. PPI ensured that the training materials being developed were responding to a genuine need and were aligned with the needs of the school staff that would be using them.

Example 2: Prevention

The intervention development in WP1b for the prevention programme (see *Chapter 3*) was informed by focus groups with 22 adolescent girls, who provided their experiences of body dissatisfaction and disordered eating and their recommendations for a preventative intervention. The intervention materials were then developed in conjunction with a panel of key stakeholders, which included a young person with a history of an ED, two young people without a history of an ED, and three secondary school teachers. Feedback provided by this panel was incorporated into the materials in an iterative process.

Example 3: Carers interventions

WP3 evaluated an intervention for carers of people with AN, which was used as an adjunct to inpatient treatment (see *Chapter 6*). It included extensive PPI, with several members of the research team having personal experiences of ED. The self-help materials (ECHO, Experienced Carers Helping Others) were developed in collaboration with patients and carers

(49). In addition, the majority of telephone coaching sessions offered during the intervention were provided by trained individuals with personal experience of ED (either having recovered from the disorder themselves or as a carer). The findings from this trial are being disseminated to the public through a website dedicated to carers of those with ED (www.thenewmaudsleyapproach.co.uk), a newsletter, the database of ED volunteers and the annual carer's conference which we run with Beat – the main national organisation for people with ED and their families.

From the above, it is clear that patient and carers were involved in designing the programme, implementing the WPs and disseminating findings. Such collaboration between researchers and service user representatives has been highlighted as exemplifying good practice in service user involvement by the Mental Health Research Network (50).

Report structure

The overarching aims of the ARIADNE programme were realised through seven independent, but integrated WPs, which are presented in detail in this report. An outline of the chapters is as follows:

- **WP1: Prevention and early intervention.** *Chapters 2* and *3* focus on prevention, detection and early intervention of ED. In *Chapter 2*, we present the development and evaluation of a learning package for school staff on how to recognise symptoms of ED, how to communicate about ED sensitively and how to assess risk. *Chapter 3* outlines the development of a teacher-delivered prevention programme for ED, and the results of a cluster randomised controlled trial (RCT) evaluating its efficacy.

- **WP2: Treatment.** *Chapters 4 & 5* focus on treatment of AN. In *Chapter 4* we present the evaluation of the Maudsley Model of Treatment for Adults with Anorexia Nervosa (MANTRA) using a large RCT in of individuals in an outpatient setting. *Chapter 5* explores the use of components of this treatment in an inpatient setting, designed as intensive modules for severe, chronic or treatment-resistant AN. Here, we evaluate this approach through case report, qualitative evaluation and a pilot trial comparing it to treatment as usual (TAU).

- **WP3: Carers interventions.** *Chapter 6* presents an intervention for those caring for individuals with AN. We present findings from a large RCT assessing the impact of a guided self-help intervention for carers of individuals with AN (Experienced Carers

Helping Others; ECHO) in addition to standard inpatient care. We report on outcomes for both carers and for patients up to 12 months post-discharge from inpatient care.

- **WP4: Physical activity in AN.** *Chapter 7* focuses on the assessment of activity levels and endocrine changes in individuals with AN. We present data from an observational study. Individuals with AN (inpatients and outpatients) are compared to individuals with anxiety and healthy controls using a range of methods, including body composition, endocrine measurements, self-report, and actimetry.

- **WP5: Relapse prevention.** *Chapter 8* focuses on relapse prevention. Here, we present a feasibility RCT on a novel e-mail guided manual-based intervention to be used in the post-hospitalisation aftercare of patients with AN.

- **WP6: Mothers with ED.** *In Chapter 9,* we present research on mothers with ED, a special population, which may need tailored services. We report findings regarding fertility difficulties in women with ED, and associations between maternal ED and their children's diet and growth trajectories.

- **WP7: Care pathways and economic evaluations.** *Chapter 10* presents results regarding service use, focusing on how access to specialist services affects rates of referrals, admissions for inpatient treatment, continuity of care, and service user experiences. *Chapter 11* uses data from ARIADNE work packages (WPs 2, 3, 5 and 7a) plus the British Cohort Study to identify the costs of services and treatments used by people with AN and to estimate its annual costs for England.

- **General discussion:** *Chapter 12* draws together the findings from the seven WPs and highlights clinical implications and recommendations for future research based on this programme.

Chapter 2. The development and feasibility testing of an eating disorders training programme for UK school staff (WP1a)

Pooky Knightsmith, Janet Treasure & Ulrike Schmidt

Abstract

Word count: 241

Work package 1a comprised of four studies.

Study One: 511 11-19 year old school students completed an online questionnaire exploring their experiences of eating disorders at school. Respondents provided actionable recommendations about improvements which could be made.

Study Two: 826 school staff completed an online questionnaire exploring their eating disorder experiences. Participants highlighted a lack of understanding and knowledge within their schools and a willingness to access training and support.

Study Three: 63 members of staff from 29 UK schools participated in focus groups to further develop the themes explored in study 2.   Five key themes emerged: Five salient themes emerged from the focus group discussions:

1. There was little general knowledge about eating disorders amongst staff
2. Mental health issues, including eating disorders, were not openly talked about amongst staff
3. School staff do not feel confident or comfortable teaching students about eating disorders
4. Where they exist, positive relationships with parents contribute to eating disorder recovery but sometimes relationships with parents are very negative.
5. More support is needed for school staff involved in the care of students undergoing eating disorder recovery.

Study Four: A one day training programme for UK school staff aimed at improving attitudes towards, confidence in supporting and knowledge about eating disorders was tested for feasibility and acceptability and was found to have a positive, significant impact with medium and large effect sizes which were maintained after three months.

Introduction

Eating disorders have a high rate of onset during adolescence (51, 52), the period during which young people attend secondary/high school. Research indicates that up to 1.5% of secondary school students suffer from a diagnosable eating disorder (53-55) and up to 15% experience sub-clinical eating disturbance (56). However, many of these cases go undetected and untreated (57).

As students spend an average of forty hours a week attending school (58) school staff are in a good position to pick up on the physical and behavioural symptoms that are present during the early stages of eating disorders (59). Furthermore, school staff are well placed to offer on-going support as young people have indicated that they are up to nine times more likely to talk to a teacher than a parent about food related difficulties (60).

Work package 1a is a series of interlinked studies designed to understand the current context of eating disorders in school and use this understanding alongside school staff and student recommendations in the development of a face-to-face training programme. The work package culminated in the training programme being feasibility tested.

Study 1: Student experiences of eating disorders within the school setting: an online survey

Methods

First and second-hand student experiences of suffering with an eating disorder at school were explored using an online questionnaire (Appendix 1.1) completed by 511 students aged 11-19 ($M = 15.4$ years, $SD = 2.3$).

Results

Multiple choice questions generated quantitative data which has been summed and recorded in Table 1.

Content analysis was used to interrogate the large amount of qualitative data produced in the form of free text responses to open questions. This is summarised in Table 2.

Thirty eight% (n=195) reported a current or previous eating disorder though 49% (n=96) had not received a diagnosis which confirms this. In total, 53% (n=115) reported being friends with a student suffering with an eating disorder.

Students' experiences and recommendations

Quantitative data are summarised in Table 1. Qualitative data are summarised in Table 2. Below, both forms of data are considered together under three salient themes which emerged during data analysis:

1. Recognition of early symptoms
2. Encouraging and supporting sufferer help-seeking
3. Providing a supportive school environment for recovery

Recognition of early symptoms

79% (n-361) of students surveyed were confident they would recognise the symptoms of an eating disorder in a friend. 30% of students had been taught about eating disorders as part of a planned programme of study at school but this was not generally well received with 82% (n=124) reporting that these lessons could have been better.

59% (n=185) Students surveyed recommended that eating disorders education needed to be improved for both students and their teachers. In free text responses, 16% (n=46) of students stated that school staff had minimal or no knowledge about eating disorders. Reducing stigma and enabling friends to recognise and respond to early symptoms were the key motivators outlined in responses.

Encouraging and supporting sufferer help-seeking

Students expressed a reluctance to highlight eating disorder concerns about a friend with a teacher with only 7% (n=33) of students stating they would be happy to do so. Several barriers for this type of help-seeking emerged including:

- Fear a teacher would dismiss their concerns
- Fear a teacher would over-react tot their concerns
- Fear that a teacher would not treat their concerns in confidence

Where school staff help was sought, students shared a clear preference for face to face discussions (73%, n=337) above writing/email (22%, n=102), or sharing concerns via phone/text (5%, n=22).

The positive impact of school staff of student outcomes was shared by 49 respondents. Four students claimed that the support provided by school staff was instrumental in preventing them from dying as a consequence of their eating disorder.

<u>Providing a supportive school environment for recovery</u>

Seventy three percent of respondents (n= 370) did not view their schools as a supportive environment for facilitating recovery from an eating disorder. Key reasons cited were:

- Bullying from peers
- Poor reintegration into school
- Staff uncertainty about how to support

Students whose experiences had been more positive outlined the important role of the school and school staff in their recovery. When asked to describe the ideal approach from school staff, respondents highlighted their desire for honesty (n=71), openness (n=19), a non-judgemental approach (n=23) and someone who felt approachable (n=29).

Table 1: Summary: Student responses to eating disorders survey –quantitative data

Could you spot eating disorder warning signs in a friend? (*n* = 458)	Yes – I have done so before	Yes – I would know the signs	I'm not sure	No		
	257 (56%)	104 (23%)	64 (14%)	33 (7%)		
Have you learnt about eating disorders at school? Was it helpful? (*n* = 499)	Taught –it was helpful	Taught – it was not helpful	I've not been taught	I'm not sure		
	27 (5%)	124 (25%)	332 (67%)	16 (3%)		
What would you do if you spotted eating disorder warning signs n a friend? (*n* = 505)	I'd help my friend if they came to me	I'd proactively offer my friend my help	I would tell a teacher	I would anonymously tell a teacher	I would talk to a trusted adult outside school	I would watch and wait
	137 (27%)	263 (52%)	33 (7%)	15 (3%)	29 (6%)	28 (6%)
If you shared your concerns with a teacher, what would you WANT them to do? (*n* = 479)	Speak with my friend	Support me in helping my friend	Talk to my friend's parents	Arrange for support from a counsellor or doctor	Listen	
	122 (25%)	216 (45%)	11 (2%)	78 (16%)	52 (11%)	
If you shared your concerns with a teacher, what would you expect them to actually do? (*n* = 474)	Speak with my friend	support me in helping my friend	Talk to my friend's parents	Arrange for support from a counsellor or doctor	Listen	

	106 (22%)	24 (5%)	229 (48%)	50 (11%)	65 (14%)
What would be your preferred way of communicating your concerns with a member of school staff? ($n = 461$)	In person	By telephone	Text/SMS/IM	Email/In writing	
	337 (73%)	5 (1%)	17 (4%)	102 (22%)	
Do you consider your school to be a supportive place for someone recovering from an eating disorder? ($n = 504$)	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
	12 (2%)	41 (8%)	81 (16%)	133 (26%)	237 (47%)

Table 2: Summary: student responses to eating disorders survey – qualitative responses

How could your school help students understand more about eating disorders?	Psychoeducation	Better services available at school	Talk more openly about eating disorders	Improve teacher knowledge	Be less judgmental
($n = 351$)	185 (59%)	68 (22%)	22 (7%)	19 (14%)	18 (7%)
	Teachers take more caring approach	School can't help	Improve access to services in school	Better resources	
	16 (6%)	10 (4%)	9 (3%)	4 (1%)	
How could your school be more supportive to students during eating disorder recovery?	Reduced stigma about eating disorders	Bespoke support	Specialist support	Nothing	Support groups
($n = 342$)	133 (43%)	72 (23%)	46 (15%)	27 (9%)	25 (8%)
	Confidentiality	Peer mentors	Promote school services		
	20 (6%)	12 (4%)	7 (2%)		
How has the school helped you or a friend in response to	They referred the case to a specialist	Staff were supportive	They spoke to parents	They were flexible re schooling	They provided on-going support

an eating disorder? (n = 169)	67 (22%)	63 (20%)	19 (6%)	10 (3%)	10 (3%)
Have you had any negative school-based experiences in response to an eating disorder? (n = 321)	No one noticed	I was punished	I wasn't appropriately consulted	I didn't get the specialist help I needed	Staff broke my confidence
	89 (27%)	31 (10%)	31 (10%)	27 (8%)	21 (6%)
	Judgmental	Lack of knowledge	Problems with the services	Negative experience not expanded upon	
	12 (4%)	10 (3%)	8 (2%)	92 (28%)	

Discussion

This was the first UK study of student experiences of eating disorders. Respondents provided valuable insight into the experiences of UK school students with eating disorders and further, provided actionable recommendations about improvements which could be made.

A strength of the study was that both male and female students were surveyed which has not previously been the norm (61).

The possibility for students to recognise and respond to early eating disorders symptoms in their friends, and for schools to provide a safe and supportive recovery environment were clearly highlighted by respondents. However, it was clear that more work is to be done if this potential is to be realised in UK schools. Psychoeducation and training for students and teachers was suggested by respondents as a key method for addressing this.

Study 2: School staff experiences of eating disorders within the school setting: an online survey

Methods

1250 UK school staff were invited to respond to an anonymous online survey exploring their experiences of eating disorders within the school setting (Appendix 1.2). 826 (66%) of the convenience sample chose to participate.

Results

Multiple choice questions generated quantitative data which has been summed and recorded in Table 3.

Content analysis was used to interrogate the large amount of qualitative data produced in the form of free text responses to open questions. This is summarised in table 4.

Below, both forms of data are considered together under four salient themes which emerged during data analysis:

1. Supporting students with eating disorders
2. Eating disorders' training and policies
3. Teaching about eating disorders
4. Reintegrating students who were absent as the result of an eating disorder

Supporting students with eating disorders

Only 40% (n=316) of respondents stated they would feel confident following up eating disorder related concerns in a student.

Eating disorders' training and policies

Sixty one percent (n=317) of respondents found policies to be an effective tool within schools. Despite this, only 32% (249) of respodents' schools had policies which made any reference to eating disorders and of these, only 5% (n=41) tookt he form of a specific eating disorders' policy.

Thirty one percent (n=160) of respondents found school policies to be ineffective in most cases, this was attributed to a lack of understanding of the role of frontline staff by senior leaders who developed policies.

Majority of respondents' schools (74%, n=583) had never provided training about eating disorders. Ninety one percent (n=316) of respondents who had not been trained said they would welcome the opportunity.

Twenty six percent (n=208) of respondents' schools had provided training. In most instances (56%, $n = 82$) this was for specialised groups of three or fewer staff.

Those staff who had received training outlined a range of benefits including:

- An increase in confidence (27%, n=39)
- Practical strategies (22%, n=31)
- Awareness of early symptoms (11%, n=15)

They also outlined suggestions for improvement, including:

- Greater depth (25%, n=24)
- More widely available (18%, n=17)
- Booster sessions (10%, n=10)

Teaching about eating disorders

Eight nine percent (n=692) of respondents reported they would not feel comfortable teaching their students about eating disorders. Reasons given for this included:

- They lacked the appropriate knowledge (57%, n=312)
- Fear of iatrogenic effects (20%, n=109)
- Students' knowledge exceeded teacher knowledge (n=64, 12%)
- Uncertainty about how to manage resulting disclosures (n=61, 11%)

Reintegrating students who were absent as the result of an eating disorder

Sixty eight percent (n=329) of respondents reported that their school had reintegrated one or more students following absence caused by an eating disorder. Twenty Four percent (n=77) of these reported receiving no training, support or advice about how best to manage this transition.

Those who had received support outlined suggestions for improvement including:

- Training more heavily tailored to the needs of the specific returning student (24%, n=25)
- Training for a wider range of people including parents and students as well as the teachers (16%, n=17)

Table 3: Summary: staff responses to eating disorders survey – quantitative data

Is there an eating disorders policy at your school? (*n* = 774)	No	Yes – within another policy	I'm not sure	Yes – we have a specific policy
	320 (41%)	208 (27%)	205 (26%)	41 (5%)
Do you think eating disorders policies are effective? (*n* = 519)	Very Effective	Effective	Ineffective	Very Ineffective
	42 (8%)	317 (61%)	148 (29%)	12 (2%)
Have you been offered eating disorders training at school? (*n* = 791)	No	Yes		
	583 (74%)	208 (26%)		
Who was the training for? (*n* = 147)	Specialist staff members (3 or less)	All school staff	All pastoral staff	All senior and middle leaders
	82 (56%)	43 (29%)	19 (13%)	3 (2%)
How was the training delivered? (*n* = 161)	Seminar	Lecture	Written materials	
	107 (66%)	37 (23%)	17 (11%)	
If you have not received any training,	Very useful	Quite useful	Not very useful	Not at all useful

do you think you would find eating disorders training useful? (*n* = 346)	160 (46%)	156 (45%)	30 (9%)	0 (0%)
Are there any current or past eating disorders cases in your school? (*n* = 530)	Yes, I am directly involved with at least one case	Yes, But I am not directly involved	No	
	266 (50%)	181 (34%)	83 (16%)	
At your school, what should a student do if they are worried a friend may have an eating disorder? (*n* = 781)	They can talk to any member of the school's staff	This is something that has never been discussed / agreed	There is a specific member of staff they should speak to	There is a system in place for anonymously raising concerns
	364 (47%)	287 (37%)	112 (14%)	18 (2%)
How comfortable would you feel teaching students about eating disorders? (*n* = 785)	I would feel very uncomfortable	I would feel uncomfortable	I would feel comfortable	I would feel very comfortable
	419 (54%)	273 (35%)	84 (11%)	9 (1%)
Has your school ever had to reintegrate a student after a period of absence caused by an eating disorder? (*n* = 487)	Yes we have	No we have not		
	329 (68%)	158 (32%)		
Did you receive any guidance about	Yes we did	No we did not		

how to support students returning following a period of absence? (*n* = 317)	240 (76%)	77 (24%)	

All questions were optional. When not all participants recorded a response to a question, percentages were calculated according to the number of respondents to the specific question.

Table 4: Summary: staff responses to eating disorders survey - qualitative responses

Perceived benefits of eating disorders training that had been completed (*n* = 142)	An increase in confidence supporting eating disorders	I learned how I can support someone with an eating disorder	I now know what warning signs to look out for	It was good to share ideas with other people	Nothing specific just generally useful
	39 (27%)	31 (22%)	21 (15%)	15 (11%)	14 (10%)
	Learned about referral processes	Raised awareness of ED	Not useful		
	12 (8%)	7 (5%)	3 (2%)		
How could the training have been improved (*n* = 96)	If it was more in depth	If it had been available to more staff	Booster sessions	The use of real case studies	Nothing the training was comprehensive
	24 (25%)	17 (18%)	10 (10%)	10 (10%)	7 (7%)
	More practical suggestions about how to support	If it was more tailored to a student causing concern	A better teacher	Information about developing policies more making referrals	Being taught in a smaller group
	7 (7%)	6 (6%)	6 (6%)	5 (5%)	4 (4%)

What staff would do next if worried that a student might have an eating disorder (*n* = 782)	I'm not sure	I'd refer to my school's policy	I would ask a more experienced colleague	I would speak with the pupil	I would talk to the pupil's parents
	316 (40%)	168 (21%)	146 (19%)	107 (14%)	25 (3%)
	I would make an external referral	I would watch and wait			
	13 (2%)	7 (1%)			
Reasons given for feeling uncomfortable teaching students about eating disorders (*n* = 546)	Too little knowledge of the topic	Fear of iatrogenic effects	It's not necessary as students have a good understanding	I wouldn't know how to manage disclosures	
	312 (57%)	109 (20%)	64 (12%)	61 (11%)	
How parents have responded to being told their child has an eating disorder (*n* = 781)	Parent has responded with denial or refusal to speak to us	Both positive and negative reactions	Difficult at first but relations improved	Parents have been angry accusing us of criticising their parenting	
	364 (47%)	287 (37%)	112 (14%)	18 (2%)	
Support that staff suggested would be helpful during the	Tailored information based	More or better training than is	More people should be involved	Training should be provided for all	Specialist support and advice on an

reintegration of a student with an eating disorder into school ($n = 105$)	on the specific student's needs	currently provided	in training (inc e.g. parents, students)	relevant staff	on-going basis
	30 (29%)	25 (24%)	17 (16%)	13 (12%)	8 (8%)
	Students need to be supported in the run up to their friend's return	Other			
	8 (8%)	4 (4%)			

All questions were optional. When not all participants recorded a response to a question, percentages were calculated according to the number of respondents to the specific question.

Discussion

This was the first UK study of school experiences of eating disorders. Respondents provided valuable insight into the experiences of UK school staff with eating disorders and further, provided actionable recommendations about improvements which could be made.

Study 3: Recommendations from school staff about spotting and supporting eating disorders

Methods

Study 3 was recruited from Study 2 participants. Of 826 respondents in study 2, there were 109 expressions of interest in participating in further studies. Sixty three of these went on to take part in the focus groups conducted in study 3.

A total of eight focus groups were held with 63 members of school staff from 29 schools in the UK. Topic guides were developed to explore school staff experience and opinion with relation to:

- School culture
- Knowledge of school staff about eating disorders
- Understanding of school staff about eating disorders
- Communication with students
- Support strategies
- Working with parents
- Working with external agencies

Results

Five salient themes emerged from the focus group discussions:

6. There was little general knowledge about eating disorders amongst staff
7. Mental health issues, including eating disorders, were not openly talked about amongst staff
8. School staff do not feel confident or comfortable teaching students about eating disorders

9. Where they exist, positive relationships with parents contribute to eating disorder recovery but sometimes relationships with parents are very negative.
10. More support is needed for school staff involved in the care of students undergoing eating disorder recovery.

There was little general knowledge about eating disorders amongst staff

In general, the staff attending the focus groups stated that their own knowledge of eating disorders was relatively good but that this was not reflected in colleagues throughout the staff body. Staff reported a lack of knowledge of the major types of eating disorder and their symptomology.

Staff also reported a lack of misunderstanding of eating disorders with many colleagues belieivng that eating disorders are a teenage phase students will grow out of. Colleagues were reported not to realsie that eating disorders are mental health issues that frequently require specialist midical and psychological intervention.

Mental health issues, including eating disorders, were not openly talked about amongst staff

Participants frequently reported a lack of open discusion about mental health issues, including eating disorders, at their schools. Many cited a fear of iatrogenic effects of discussing eating disorders either amongst staff or with students whislt others shared senior management concern that being seen to be focusing on eating disorders would result in potential students and parents gaining a negative impression of the school.

School staff do not feel confident or comfortable teaching students about eating disorders

Staff expressed a lack of confidence and knowledge about how to talk safely to students about eating disorders both in the context of speaking directly to sufferers and in the context of teaching students about eating disorders as part of a structured curriculum. Staff feared saying or dong the wrong thing and in so doing promoting eating disordered behaviours either in students during their recovery or amongst the general student population.

Where they exist, positive relationships with parents contribute to eating disorder recovery but sometimes relationships with parents are very negative

Participants highlighted the importance of the role of the parent during recovery and the need for schools and parents to work closely together during the period of recovery. However, many staff also outlined incidents which illustrated very negative school-parent relationships. Negative responses were reported most often as a result of the initial disclosure from school to parents about a child's eating disorder and negative reactions from parents included :

- Parents seeing the school as interfering unnecssarily
- Parents believing the school was accusing them of poor parenting
- Parents suggesting the school was over-reacting

Focus group participants highlighted the importance of the initial conversation with parents as a key time for setting the tone for the school-parent relationship.

More support is needed for school staff involved in the care of students undergoing eating disorder recovery.

Focus group participants highlighted the need for further support for school staff during the recovery period. They expressed a need for practical guidance on a range of topics including :

- Student participation in sports, exercise or physical education lessons
- Supporting mealtimes
- Academic expectations including expectations around homework

Discussion

Focus group participants provided detailed, actionable insights into the current of confidence, understanding, knowledge and attitudes of UK school staff from a range of geographically and socio-economically diverse schools.

Whilst the group reported themselves to be more than usually interested in and informed about eating disorders and ohter mental health issues, they drew widely on the knowledge, experience and attitudes of colleagues during the course of hte focus groups.

Development of content and outcome measures

A day long training programme for school staff on the topic of eating disorders was developed in line with the NICE Principles of Effective Behaviour Change Interventions (62). Data from studies 1, 2 and 3 was drawn on significantly during programme development. Furthermore, school staff and clinicians were heavily involved in the authoring and piloting of training materials in order to ensure the resulting training programme was relevant and practical for use within a UK school setting whilst also drawing on the most recent evidence based practice.

Content Outline

Based on school staff feedback about what is feasible in terms of INSET training the intervention was designed to be delivered in four 90 minute sessions which could be delivered within the space of one day.

Each ninety minute session had clearly designed objectives and focus. These were:

- **Session one: Eating disorders introduction**
- **Session Two: When and how to talk to students causing concern**
- **Session Three: Working with parents, staff and students**
- **Session Four: Providing a supportive environment during recovery**

Outcome Measures

An outcome measure of school staff eating disorders attitude, confidence and knowledge were developed for using during the current study as there was no existing tool. The new tool drew on existing measures of GP attitudes (Currin, Waller, & Schmidt, 2009) and the feedback of school staff and students shared in studies 1 to 3.

A self-report style tool was develped which captured attitudes, confidence and knowledge about eating disorders. A copy of the self-report measure is included in *Appendix 1.3*.

Study 4: Feasibility study of a one day eating disorders training programme for UK secondary school staff

Methods

45 members of UK school staff completed a one day face to face training programme designed to improve their knowledge about, attitudes towards and confidence in managing eating disorders. Participants completed self-report measures of knowledge, attitudes and confidence at the beginning of the day, before training commenced (T_1, baseline), at the end of the day, once training was completed (T_2, post-intervention), and again 3 months later (T_3, follow-up).

The significance of intragroup changes was determined using a generalised estimating equations (GEE) models.

Results

The full results of the statistical analyses are shown in Table 5 and Table 6. There was a statistically significant improvement (all p values < 0.001) in participants' self-reported knowledge, attitude and confidence scores post intervention (T_2) compared to baseline (T_1) with a large effect size on all three comparisons (63). These differences were maintained at the 3 month follow-up (T_3) and there was no significant difference between the knowledge, attitude or confidence scores measured post intervention (T_2) and at the three month follow-up (T_3).

Participants all completed a post course evaluation form designed to assess the acceptability of the intervention. All delegates ($n = 45$) considered the course either good (16%) or very good (84%) in terms of course content, course materials and for providing practical strategies they could use at school.

Table 5: Estimated means and standard errors

Measure	Baseline (T_1)		Post Intervention (T_2)		Follow-up (T_3)	
	n	m (*se*)	n	m (*se*)	n	m (*se*)
Knowledge	45	17.1 (0.76)	45	29.9 (0.78)	45	29.3 (0.76)

Attitude	45	29.9 (0.17)	45	37.9 (0.56)	45	37.2 (0.53)
Confidence	45	24.9 (1.44)	45	48.7(1.40)	45	47.0 (1.38)

Table 6: Post hoc analyses

Measure	Baseline (T_1) to Post Intervention (T_2)				
	B	Effect Size	95% Confidence Interval		Hypothesis Test
			Lower	Upper	Sig.
Knowledge	12.8	0.8	11.3	14.4	<0.001
Attitude	8.1	0.8	7.0	9.1	<0.001
Confidence	23.8	0.8	21.2	26.4	<0.001
Measure	Baseline (T_1) to Follow-up (T_3)				
	B	Effect Size	95% Confidence Interval		Hypothesis Test
			Lower	Upper	Sig.
Knowledge	12.2	0.7	9.9	14.5	<0.001
Attitude	7.4	0.8	6.3	8.4	<0.001
Confidence	22.1	0.8	17.9	26.3	<0.001

Discussion

A one day training programme for UK school staff aimed at improving attitudes towards, confidence in supporting and knowledge about eating disorders was tested for feasibility and acceptability and was found to have a positive, significant impact with medium and large effect sizes which were maintained after three months. However, the study was limited by the use of outcome measures which were entirely subjective / self-reported and in the lack of a longer term measure of maintenance of positive outcomes.

General discussion

Strengths

All four studies conducted as part of this work package were the first of their type within the UK setting.

The contribution of male viewpoints is a significant strength of the current work as this has not previously been the norm (61).

A further strength of the studies was the large number of participants for studies of this type, (511 student survey responses in study 1 and 826 school staff responses in study 2) and the depth of responses provided by these participants.

A key strength of study 4 was the immediate and lasting impact of the intervention on participant attitudes, confidence and knowledge about eating disorders despite its brevity. A programme which took longer to deliver or whose affects were not lasting would not be feasible or relevant for use in UK schools. Data collection at baseline, post intervention and 12 weeks post-intervention is recommended but not widely practised (64, 65).

Limitations of the studies

It was not feasible to include both experimental and control groups within each school participating in study four due to the possibility of trial arm contamination resulting from sharing of information between school staff, especially post intervention. In future studies, a stepped wedge design could be employed to overcome this with every participant completing both the control and intervention conditions.

The positive outcomes reported from study four in terms of an improvement in staff attitudes, confidence and knowledge were based entirely on self-report measures. Future studies could include some additional objective measures.

Study four looked only at school staff outcomes; the impact of the intervention was not extrapolated to explore the impact on student outcomes. Similar studies have similarly failed to provide such evidence (64, 65) but appropriate measures should be considered for inclusion in future studies.

Future directions

The implementation of a fully powered stepped-wedge design in order to fully test the training programme developed in study four is a key future direction. Another possibility for exploration is the development of online training materials that could be accessed remotely in order to increase the reach and cost effectiveness of the programme.

Conclusions

The aim of the current work package was to develop and feasibility-test an eating disorders training programme for school staff aimed at improving attitudes, confidence and knowledge.

This aim was achieved through a series of studies which drew extensively on the experiences and understanding of UK school staff and students in relation to eating disorders.

The work of all 4 studies was unique within the UK setting and the outcomes were promising and provide clear pathways for future research.

Chapter 3. Body image in the classroom: Developing and testing a teacher-delivered eating disorder prevention programme by clustered randomised controlled trial. (WP1b)

Helen Sharpe, Janet Treasure & Ulrike Schmidt

An abbreviated version of this chapter has been published in the British Journal of Psychiatry (66).

Abstract

Word count: 236

Objectives: To design and evaluate a universal prevention programme for eating disorders in secondary schools.

Trial design: Clustered randomised controlled trial comparing intervention lessons to curriculum-as-usual control.

Participants: Students in years 8 & 9.

Intervention: Six-session Me, You & Us programme delivered by teachers.

Outcomes: Questionnaires at baseline, post-intervention and three month follow-up assessing body esteem (primary outcome), eating pathology, thin-ideal internalization, appearance conversations, peer support, depressive symptoms, and self-esteem.

Randomisation: Unrestricted randomisation of intact classes using random number generator.

Blinding: Teachers, students and researchers were not blinded to group assignment.

Numbers randomised: 16 classes were allocated to intervention (9 classes, 261 students) or control (7 classes, 187 students). No participants dropped out.

Results: There were significant between group differences in body esteem favouring the intervention group at post-intervention ($d = 0.12$) and three month follow-up ($d = 0.19$). There were also significant between group differences in thin-ideal internalization ($d = 0.17$, maintained at follow-up, $d = 0.16$), and self-esteem ($d = 0.20$, not maintained at follow-up). There were no between group differences for the other outcomes. Fidelity to intervention material and acceptability of the programme varied across the three schools.

Harms: There was no evidence of reduction in body esteem.

Conclusions: Me, You & Us improved body esteem, thin-ideal internalization and self-esteem, but not other outcomes. Further work to increase efficacy across the range of outcomes and improve fidelity would be valuable.

Trial registration: ISRCTN42594993.

Introduction

Eating disorders are valuable targets for prevention because of their poor outcomes, elevated mortality rates and associated personal and financial costs (67-72). Universal prevention programmes are a useful element of the prevention portfolio as they allow us to tackle elements of the social environment that are known to be risk factors for eating disorders, such as perceived pressure from peers towards thinness (73, 74). Universal interventions also do not face some of the difficulties of selective programmes, namely: the stigma associated with participating and the low uptake of those identified as being at risk (75).

Secondary school teachers are in a unique position to deliver prevention material widely and with minimal costs, as they have regular contact with almost all of the adolescent population. However, given the difficulties of achieving randomisation in the school setting, very few teacher-delivered interventions have been evaluated by means of randomised controlled trial (76-81), and none have done so within the UK. In addition, several of these trials have small sample sizes making them underpowered (77, 80, 81). The current state of evidence regarding the efficacy of teacher-delivered interventions for eating disorders is therefore very poor. Given the potential scope for these universal interventions, this lack of high quality evidence is problematic.

In 2012 the UK All Party Parliamentary Group on Body Image recommended that all schools (primary and secondary) include mandatory lessons on body image in response to the high levels of body dissatisfaction and disordered eating in the adolescent population (82). However, the lack of evidence base in this field means teachers and school staff are unable to make evidence-based decision about how best to implement this recommendation. This has resulted in some programmes, such as *Media Smart* (developed by the Advertising Standards Agency, www.mediasmart.org.uk/resources/bodyimage) being widely disseminated without any evidence for their efficacy. This is problematic as, aside from the potential for wasted resources, some trials of interventions for eating disorders (83) and depression (84) in schools have found evidence of detrimental effects. There is therefore a need for safe and effective, evidence-based eating disorder prevention programmes that are deliverable by school teachers.

This study describes the evaluation of a universal teacher-delivered eating disorder prevention programme called "Me, You & Us". The intervention material was based on identified risk factors for eating disorders and body dissatisfaction (6, 85, 86): thin-ideal

internalization; appearance conversations with friends; negative affect; and low self-esteem. Intervention development was supported by a panel of experts and stakeholders, including PPI representatives: clinicians and researchers specialising in eating disorders; teachers and school nurses; and young people with and without a history of eating disorders.

In addition, three focus groups with 21 adolescent girls were used to determine young people's experiences of body dissatisfaction and eating pathology, their understanding of the aetiology of these problems, and their recommendations for preventative strategies (87). These groups revealed that young people largely endorse a socio-cultural approach to body dissatisfaction and eating disorders, in which media literacy and building networks of support are seen as helpful. These recommendations informed intervention development with the aim of improving the acceptability of the material produced.

Based on this review of empirical literature, including previous universal interventions, and the consultation period, a facilitator's guide and student workbook were developed (88). There were six, interactive 50 minute lessons, with the following topics.

Lessons 1 & 2: Media literacy
The aim of the first two lessons was to help participants to critique media presentations of ideal beauty through exploring how conceptions of beauty have varied over time and place, what messages are hidden in media images, and how to take action.

Lessons 3 & 4: Fat talking
Lessons three and four focused on perceived peer pressure towards thinness, introducing the concept of fat talking, and examining why we might fat talk as well as possible consequences. The lessons went on to challenge negative appearance-related commentary through exploring the giving and receiving of compliments.

Lesson 5 & 6: Personal strengths and wellbeing
The remaining lessons focused on tackling negative affect and low self-esteem through learning about personal strengths and how to use them. Simple exercises to promote wellbeing were explored in the final lesson, including writing a gratitude letter and carrying out small acts of kindness.

Aims and hypotheses

The aims of this study were to assess the efficacy, feasibility and acceptability of *Me, You & Us*, a teacher-delivered universal prevention programme for eating disorders. The following hypotheses were generated:

Main hypothesis:

1. Students receiving the intervention will show significant improvements in body esteem, internalisation, peer support, appearance conversations, depressive symptoms, self-esteem and eating pathology compared to students in the control group at post-intervention and at a three month follow up.

Subsidiary hypotheses:

2. Students will find the material in the intervention acceptable, in that they will report enjoying the lessons and perceive them as useful.
3. It will be feasible to train usual secondary school teachers to deliver an eating disorder prevention programme from a manual and student workbook with high fidelity.

The aims of the trial were to determine the acceptability, feasibility and efficacy of this universal prevention programme for eating disorders.

Methods

Trial design

The study used a cluster randomised controlled trial design with intact classes of students allocated in a 1:1 ratio to intervention or control arms (trial registration: ISRCTN42594993, including protocol).

Participants

Eligibility criteria

Participants were adolescents in year 8 or year 9 in a secondary school in the United Kingdom. Secondary schools provided the point of access to participants. Schools were eligible to take part if:

- The school was based in the United Kingdom.
- The school had classes of students in years 8 and/or 9.
- The school had a sufficiently flexible timetable to manage random allocation of lessons to participating classes.

Participants were eligible to take part if:

- They attended grade 8 or grade 9 in a participating secondary school
- They were deemed by a member of school staff (head teacher, form teacher, school nurse) to have sufficient English language reading ability to be able to comprehend consent procedures and manage written questionnaires.

Settings and location of data collection

All data were collected within the school setting. School staff administered questionnaires within regular school hours, based on protocols provided by the researcher. Data collection took place between September 2011 and May 2012.

Intervention

The programme involved six, 50-minute lessons which teachers delivered to existing classes. The intervention content was described in a Facilitators' Manual and Student Workbook, both of which are available from the first author (HS). As discussed above, the material targeted risk factors for eating disorders and body dissatisfaction, namely: thin-ideal internalisation, peer factors, depression and low self-esteem (6, 86, 89). Participating teachers received a standardised two-hour session, involving education about eating disorders and introduction to the Me, You & Us manual.

The control group received their usual curriculum. The content of these lessons were not determined by the research team.

Outcomes

Age, ethnicity and parental education were provided by participant self-report one week before the intervention began ('pre-intervention'). Participants also completed an eating disorder screening tool, the Eating Disorder Diagnostic Scale (90), which identifies DSM-IV diagnostic criteria for anorexia nervosa, bulimic nervosa and binge eating disorder.

All primary and secondary outcome measures were administered at pre-intervention, one week following the intervention period ('post-intervention') and at approximately three months following the intervention period ('three month follow up').

Primary outcome

Body esteem

Body esteem was assessed using the Body Esteem Scale for Adults and Adolescents (91), a 23 item self-report measure in which participants have to rate the frequency with which they agree with statements about confidence with their appearance on a five point Likert scale. Note that higher scores represent greater body esteem (i.e. lower body dissatisfaction)

Secondary outcomes

Presence of binge eating

The presence of binge eating was assessed using the Eating Disorder Diagnostic Scale (90) and was defined as self-reported binge eating with loss of control at least once a week for three months.

Presence of compensatory behaviours

Compensatory behaviours were also assessed using the Eating Disorder Diagnostic Scale (90) and were defined as self-reporting of at least one of the following behaviours at least once per week for three months: vomiting, laxative/diuretic use, meal skipping, or excessive exercise.

Thin ideal internalisation

The extent to which participants adhered to the media portrayal of the ideals of thinness was assessed using the *General Internalisation* subscale of the Sociocultural Attitudes Towards Appearances Scale – 3 (SATAQ - 3, 92). The General Internalisation subscale consists of nine items about appearances and the media (TV, magazines, films), such as "I would like my body to look like the models who appear in magazines", with which participants have to agree or disagree on a five point Likert scale. Higher scores represented greater thin ideal internalisation.

Appearance conversations with peers

The frequency with which participants engaged with friends on the topic of appearances was measured using the Appearance Conversations with Friends Scale (ACFS, 93). The five items are designed to assess "how often students talked with their friends about expectations for their bodies and for appearance enhancements" (93, p. 329) and take the form of statements such as "my friends and I talk about the size and shape of our bodies" with which participants have to agree or disagree on a five point Likert scale. Higher scores represent more frequent appearance conversations.

Peer support

Perceived social support was measured using the Friend subscale of the Multidimensional Scale of Perceived Social Support (MSPSS, 94). This four item scale assesses perceived support from friends through responses on a seven-point Likert scale to items such as "My friends really try to help me". Higher scores represented greater perceived social support.

Depressive symptoms

Depressive symptoms were assessed using the Depression subscale of the short version of the Depression, Anxiety and Stress Scale (DASS-21, 95). The DASS-21 Depression Subscale is a seven item scale in which participants are required to state how often particular statements, for example "I felt that I had nothing to look forward to", applied to them over the past week. Higher scores represent greater depressive symptoms.

Self esteem

A single item – "How positive do you feel about yourself?" - was used to assess self-esteem. Participants were required to respond on a five point Likert scale from 'Not at all positive' to 'Very positive'. Higher scores represent higher self-esteem.

Acceptability

The programme's acceptability was assessed using two five point Likert scales. The first asked: "How much did you enjoy Me, You & Us?", and the second asked: "How useful did you find Me, You & Us?". The Likert scales ranged from 'Not at all' to 'Very much'. Higher scores represent greater acceptability.

Fidelity to intervention guide

In order to determine fidelity to the intervention manual, two lessons were observed and rated in each school against adherence to planned content. Each activity in the Facilitator's Guide was scored as 'completed', or 'not completed'. Free text was used to note whether any additional material was covered.

Sample size

To account for clustering, the sample size calculation was increased by an inflation factor (1 + (average cluster size − 1) ICC). The inflation factor for this trial was based on a small intraclass correlation (ICC = 0.05) (96). With an average class size of 28 students the estimated inflation factor was 2.35.

G*Power 3 was used for sample size calculations (97). Assuming a 1:1 ratio, a small effect size (d = 0.20) (98) and power set to 0.80, the basic sample size requirement was 394 participants per group, which increased to 926 per group when the estimated inflation factor was taken into account.

Randomisation and blinding

Intact classes were randomly allocated to intervention and control arms. As classes were enrolled into the trial, an unrestricted random allocation was generated by an online random number generator (99). One researcher (HS) carried out the enrolment of classes, the generation of the random allocation sequence and the allocation of classes to conditions. Participants' allocation in trial arm was based on their class membership. Informed consent for participants was obtained from all participants' parents/carers following randomisation. In addition, participants provided written assent post-randomisation, when completing the pre-intervention questionnaire measures.

The trial design precluded blinding of school staff or students participants as intervention materials such as the student workbooks would have been identifiable to staff and students as being distinct from their usual curriculum. Researchers were also unblinded.

Statistical analyses

Full details of statistical analyses, including managing if missing data are reported elsewhere (66). All analyses were based on originally assigned groups. The main hypothesis was tested using linear and logistic mixed effects models. Two continuous outcomes that were not normally distributed (depression, peer support) were dichotomised for all analyses.

In addition to significance testing, effect sizes (*d*) for continuous outcomes were calculated using the differences in adjusted means at each time point. Reliable and clinically significant changes was also computed (100) using reliability data and clinical cut offs from previous work (101).

Results

Participant flow and characteristics

Three schools agreed to participate in the trial. One additional school refused participation because the did not want to trial previously untested resources. Each of the schools was state-maintained and had 100% female intake. The three schools varied in their average level of

deprivation (free school meal eligibility ranged form 2% to 24%) and in the ethnic background of their students (the percentage of students of black and ethnic minority backgrounds ranged from 28% to 77%). Random allocation of 16 intact classes from year 8 or 9 in these schools resulted in 9 classes allocated to the intervention arm and 7 classes allocated to the control arm. Of the 479 students from these classes, 31 were excluded because of lack of parental consent. This resulted in 261 students in the intervention arm and 187 students in the control arm. Between 92% and 98% students provided data at each data collection point. All missing data were due to school absence. No participants withdrew from the trial.

There were no significant differences between the two trial arms at the beginning of the trial. Participants had a mean age of 13.06 years (sd = 0.59) in the intervention group and 12.99 (sd = 0.54) years in the control group. Equal proportions of participants came from ethnic minority backgrounds (intervention = 47%, control = 53%), and had parents with university level education (intervention = 76%, control = 78%). There was also no difference on reports of body esteem (intervention: m = 2.30, sd = 0.75, control: m = 2.27, sd = 0.70) or across any of the other clinical outcomes for the trial. Eight participants scored above the cut off in the ED screening tool and so were excluded from analyses on the grounds that the aim of the programme was prevention of future difficulties.

Acceptability and feasibility

Students in the intervention arm were asked to rate how useful and enjoyable they found the lessons in the intervention. Results are shown in Table 7. Looking across both ratings of lessons being enjoyable and useful, the acceptability are notably higher in two schools (A and C) compared with the third school (B). Whereas few students (3% to 16%) in schools A and C rated the programme negatively, this figure was nearer 50% for school B. These findings mirror the results of the feasibility assessment, in which the teachers' fidelity to the intervention manual were assessed. That is, a greater amount of intervention content was delivered in schools A and C compared with in school B (78% compared with 50%).

Table 7: Acceptability of intervention lessons by school

	School A (%) n = 31	School B (%) n = 79	School C (%) n = 80
Enjoyable			
Negative	3	48	9
Neutral	34	36	48
Positive	63	16	43
Useful			
Negative	10	51	16
Neutral	39	30	41
Positive	51	19	43

Body esteem

Results from the mixed effects models showed an overall marginal effect of the intervention on improvements in body esteem ($b = 0.09$, $se = 0.05$, $p = 0.08$). Post-hoc analyses at each time point showed a marginal difference between the groups at post-intervention (intervention: $m = 2.31$, $se = 0.32$; control: $m = 22.2$, $se = 0.39$, $p = 0.07$) and a significant difference between the groups at three-month follow up (intervention: $m = 2.37$, $se = 0.32$, control: $m = 2.22$, $se = 0.39$, $p = 0.006$). In each case the results favoured the intervention over the control condition. The effect sizes for these group differences were small ($d = 0.12 - 0.19$).

Reliable and clinically significant change between baseline and post-intervention was calculated separately for those above and below the clinical cut off at baseline. As this was a community sample, few participants were above the clinical cut off at baseline (n = 60). In those above the cut off initially, 50% (n = 17) of participants in the intervention group showed clinically significant improvement, compared with 38% (n = 10) in the control group. However, this difference was not statistically significant ($\chi^2(1) = 0.79$, $p = 0.37$). When considering reliable change, 32% (n = 11) participants in the intervention group showed reliable improvement compared with 8% (n = 2) in the control group. This difference was statistically significant ($\chi^2(1) = 5.97$, $p = 0.02$).

Considering those participants that began the trial in the normal range for body esteem, it was notable that there were no participants that experienced clinically significant worsening of symptoms. Some participants did, however, show reliable improvements in body esteem. In the intervention group 12% participants (n = 20) experienced reliable improvement compared with 4% in the control group (n = 4). This difference was statistically significant ($\chi^2(1) = 6.58$, $p = 0.01$).

Secondary outcomes

Linear mixed effects model for continuous secondary outcomes showed that there was a main effect of group for thin-ideal internalisation ($b = -1.53$, $se = 0.74$, $p = 0.04$) and self-esteem ($b = 0.19$, $se = 0.09$, $p = 0.04$). There was no significant main effect for appearance conversations ($b = -0.04$, $se = 0.32$, $p = 0.90$). For thin-ideal internalisation, looking separately at each time point showed significant differences between the groups at both post-intervention (intervention: m = 21.94, se = 0.47, control: m = 23.47, se = 0.57, $p = 0.04$), and at the three month follow up period ($\chi^2(1) = 3.84$, $p = 0.05$). At each time point the results favoured in the intervention. For self-esteem, the comparisons between the groups at each of the time points revealed a significant difference at post-intervention (intervention: m = 3.52, se = 0.06, control: m = 3.33 se = 0.07, $p = 0.04$), but no difference by three months follow up (intervention: m = 3.47, se = 0.06, control: m = 3.34, se = 0.07, $p = 0.15$).

Logistic mixed effects models were used to explore intervention effects for binary outcomes. There were no main effects of group for binge eating ($OR = 4.44$ [0.39 – 51.22], $p = 0.23$), compensatory behaviours ($OR = 1.69$ [0.74 – 3.89], $p = 0.22$), peer support ($OR = 1.40$ [0.64 – 3.06], $p = 0.40$), or depressive symptoms ($OR = 1.49$ [0.46 – 4.78], $p = 0.50$). Rates of each of these outcomes at each time point are reported in detail elsewhere (66).

Discussion

This study described the designing and first rigorous evaluation of a teacher-delivered eating disorder prevention programme in UK secondary schools. The results suggest that the approach is feasible and that a programme of this kind can have benefits for adolescents' mental health.

The programme produced significant improvements in participants' body esteem compared with their peers who received their usual school curriculum, and this impact was maintained through the three month follow up period. The programme also improved several of the

secondary outcomes. First, thin-ideal internalisation was reduced, meaning that the participants were less likely to endorse social ideals associated with thinness. Second, self-esteem was greater in those that received the intervention, although the effects were no maintained after the post-intervention assessment. In contrast to these findings, there were no effects for eating pathology, appearance conversations, peer support, or depressive symptoms. There was also clear evidence that intervention delivery and reception varied substantially between the three schools. This suggests that understanding the best way to support delivery of materials such as these in a wide range of schools is a key aspect to take forward from this research.

It is difficult to compare these results with previous work difficult because most body image interventions in schools have not been delivered by teachers but rather by external expert facilitators (98, 102). The small effect sizes found in this trial are in line with work outside of the UK in which teacher-delivered interventions have been tested (76, 103). Existing work has also reported similar null findings for the broader impact of eating disorder prevention programmes. For example, other work has found like effect on depressive symptoms despite some content dedicated to this factor (76, 80). Given that interventions focusing specifically on depression are more intensive, it may be that the problem is one of dosage (104). Similarly, few teacher-delivered prevention programmes has successful impacted upon eating pathology (79, 80) although one study with considerably more intensive teacher training has shown promise in this area (77).

Strengths and limitations

A number of factors limit the conclusions of this trial. First, there was a risk of control group contamination, due to random allocation of classes within the same school. Second, we did not use an active control condition. Potentials for sham interventions that have been used in previous similar trials include activities such as expressive writing (105), educational brochures (106), or healthy eating programmes (107). Third, the sample size recruited was below that required for desired statistical power. Post-hoc estimates of achieved power using the effect size for the primary outcome at three month follow up ($d = 0.19$), show that the trial only had 49% power to detect group differences. Fourth, the assessment of intervention fidelity was coarse (two lesson observations per school). Ideally the trial would have involved recording all sessions and having these rated by independent researchers. Finally, the follow

up period in this trial was limited to three months. Valuable information about whether effects are maintained in the medium-long term would be gained from longer follow up.

The generalizability of the results was bolstered by the fact that the schools involved represented a wide range of different participants, including many from ethnic minority backgrounds as well as a range of economic backgrounds. It is also of significance that the trial was conducted in state-funded schools, and was not delivered by specialist school staff. However, it should be pointed out that the reliance on girls' schools does limit the generalizability of these findings as typical state-maintained schools in the UK are co-educational. Replication of these findings in co-educational schools is a priority going forwards with this work.

Conclusions

Overall this study suggests that it is possible to design a teacher-delivered eating disordered prevention programme that is efficacious, manageable for teachers and liked by students. The between-school differences in acceptability and fidelity suggest that further work is needed to increase the suitability of the materials across a range of school settings and also to examine best practice around training teachers for taking on the delivery of this programme. Efficacy was not found across all outcomes and so there was also scope for improvements to the materials where intended impacts were not observed. In addition, further trials will be essential to replicate these findings and to ensure that materials provided for schools are a safe and effective use of school resources in tackling eating disorders.

Chapter 4. A randomised controlled multi-centre trial comparing the Maudsley Model of Anorexia Nervosa Treatment for Adults (MANTRA) with Specialist Supportive Clinical Management (SSCM) in Outpatients with Broad Anorexia Nervosa

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Abstract

Word count: 246

Objectives: To assess the efficacy of a new psychological treatment for Anorexia Nervosa (AN) (Maudsley Model of Anorexia Nervosa Treatment for Adults, MANTRA) versus specialist supportive clinical management (SSCM) in a randomised controlled trial.

Trial design: Multi-centre two-arm superiority trial.

Setting: Four specialist eating disorder services within the south of England

Participants: Adult outpatients, aged between 18 and 65 years, meeting DSM-IV criteria for AN or AN-type eating disorder not otherwise specified (EDNOS-AN) with a Body Mass Index (BMI) below 18.5 kg/m^2.

Intervention: 20 once weekly treatment sessions of MANTRA or SSCM (extended to 30 sessions in those with BMI below 15 kg/m^2 and optional extras (carers sessions, dietetic sessions).

Outcomes: Primary: BMI, Secondary: Eating Disorder Examination, depression, anxiety and clinical impairment; neuro-and social-cognitive measures; rates of recovery; and utilisation of other services. Outcomes were assessed at baseline, 6-months and 12-months.

Randomisation: Completed independently from trial team using a restricted stratified randomisation algorithm with 1) BMI > or $\leq$ 15 kg/m^2, 2) AN-subtype, 3) previous ED admission as stratifiers.

Blinding: Research assessors were blind, but patients and therapists were not blinded to treatment allocations.

Numbers randomised: 72 patients allocated to MANTRA and 70 allocated to SSCM.

Results: There was no difference in outcome between groups, In both treatments patients showed significant improvements in BMI, eating disorder symptoms, and other clinical outcomes. Patients rated MANTRA as more acceptable and credible than SSCM at 12 months.

Harms: One SSCM patient died during treatment.

Conclusions: Both MANTRA and SSCM can be used as out-patient treatments in adults with AN.

Trial registration: ISRCTN67720902

<u>Introduction</u>

Anorexia Nervosa (AN) is a severe mental disorder which has the highest rate of premature death of any psychiatric disorder. It also is accompanied by much somatic and psychological co morbidity and quality of life is poor (109, 110) (110). Positive treatment outcomes are difficult to achieve because the disorder is valued by sufferers. In addition, the anxious and obsessional personality traits which patients commonly present with impede recovery. Neuro-cognitive and socio-emotional functioning are often impaired (16, 111, 112) which makes engagement in treatment an even greater challenge.

AN puts a great burden on families (113) as relatives are typically closely involved in supporting the person with the illness. Family members carry a burden comparable to that of carers of individuals with psychosis (48). The financial burden for the health service is also substantial with the cost per case of AN equating to that of schizophrenia (45, 46). Recent reports from the UK and Australia point to considerable costs of eating disorders to the healthcare sector, sufferers and their families (114-116).

Psychotherapy is the recommended first line treatment for most people with AN, but treatment outcomes greatly depend on the stage of the illness. For adolescents with a shorter duration of illness the response to the usually family based psychological treatment is excellent (117). In contrast for adults with a longer illness duration, treatment outcomes are much less positive and dropout rates are high (118). Different professional bodies on both sides of the Atlantic have highlighted the need to develop better treatments for adults with AN (119-122).

A Cochrane review of outpatient treatment for AN identified seven small and underpowered treatment trials, two of which included children or adolescents (123). No treatment approach was consistently better than any other. To date, only one sufficiently powered randomised controlled trial (RCT) has been conducted. This compared individual psychodynamic therapy, cognitive behaviour therapy and an optimised treatment as usual. Here once again, no clear differences in weight outcomes were found between groups at the end of treatment.

A potential reason for the unimpressive treatment outcomes in adults with AN is that treatments that have been tested in RCTs were originally developed in the context of other disorders and have then been modified for use in AN. Available treatments are therefore not suitably tailored to the requirements and/or specific maintenance factors of AN. In an

attempt to rectify this problem, we have developed a new treatment for AN, based on our group's research into neuro-cognitive, social cognitive and personality characteristics of these patients (20, 124, 125), the Maudsley Model of Treatment of Adults with AN (MANTRA). This treatment is unique in including maintenance factors that are intra-personal or inter-personal. It also includes therapeutic strategies to address these. The treatment is manualised and contains a number of treatment modules. The content of these can be tailored to the needs of each individual.   This novel treatment is compared here against a gold standard comparison treatment, Specialist Supportive Clinical Management (SSCM). SSCM was designed as a comparison treatment in a small trial of outpatient therapies for AN (126) and was found to be superior on a range of outcomes compared to cognitive behavioural therapy (CBT) and interpersonal therapy (IPT) in the treatment of adult AN.

Aims

- The central aim of this work is to test the efficacy, cost and cost-effectiveness of MANTRA in adult outpatients with AN versus SSCM using a randomised controlled design. (Only efficacy data are reported here, cost and cost-effectiveness data will be reported elsewhere).
- The subsidiary aim is to assess the impact of the experimental treatment on the requirement for any intensive (i.e. day-care or in-patient treatment) and to identify mediators and moderators of treatment outcome. (These will be reported elsewhere).

Hypotheses

- MANTRA will be superior to SSCM in producing higher weight increase and greater reduction in eating-disorder symptoms in adults with AN at 6 and 12 months.
- MANTRA will be more cost-effective than SSCM, being less costly at 6 and 12 months. Specifically, MANTRA patients will need fewer and briefer hospitalisations during the study period compared to SSCM. (Only the hospitalisation aspect of this hypothesis is addressed here, the full cost- and cost-effectiveness analysis will be reported elsewhere).

Methods

The methods presented here are taken from the published MOSAIC Trial Protocol (127).

Trial design

This is a superiority trial conducted in four NHS specialist eating disorders Units. The trial evaluated the efficacy and cost-effectiveness of MANTRA versus SSCM, in consecutively referred adult out-patients with AN. Patients were allocated to one of two treatment arms: MANTRA or SSCM. Further details on the randomisation procedure are given below.

Outcomes were measured pre-randomisation, at 6 months post-randomisation (i.e. designed to broadly coincide with the end of weekly treatment) and at 12 months post-randomisation (follow-up). Outcomes were assessed by researchers who were not involved in the treatment and efforts were made to keep researchers blind to patients' treatment allocation. As much as possible, patients who had terminated treatment early were followed-up to enable intention-to-treat (ITT) analysis.

Ethical approval

We obtained ethical approval for the MOSAIC Trial from Central London REC 4, National Research Ethics Service, Royal Free Hospital, London, NHS REC Reference: 10/H0714/9. All participants provided informed written consent prior to entering the study. The study was conducted in compliance with the Helsinki Declaration.

Participants

Inclusion criteria

Consecutive patients referred for out-patient treatment to one of the participating centres by their general practitioner (GP) were offered participation if they were:

a. between 18 and 60 years old,
b. had a BMI of ≤ 18.5 kg/m^2,
c. had a DSM-IV diagnosis of AN or EDNOS. We defined EDNOS as in the meta-analysis by Thomas et al. (128) and included individuals who fulfilled all diagnostic criteria of AN, with the exception of the weight criterion; those who still had menstrual bleeds; those who did not have a fat phobia; and those with a partial AN syndrome (i.e. they had features of AN but missed two or more of the four diagnostic criteria).

The meta-analysis by Thomas and colleagues(128) shows that EDNOS patients with a more lenient BMI cut-off and without amenorrhoea are very similar to more narrowly defined AN. The BMI cut-off of 18.5 kg/m^2 was selected, to be concordant with the World Health

Organisation's cut-off for being underweight. Additionally, this cut-off was also used in our previous studies by our group and others (127, 129, 130).

Exclusion criteria

We excluded patients if they had: severe, medically unstable AN which required inpatient treatment (122), poor command of English and thus unable to understand assessment and treatment; learning disability; significant other mental or physical illness which required intervention (e.g. psychotic illness or diabetes mellitus); alcohol or substance dependence or pregnancy.

We did not exclude patients on stable doses of antidepressants, defined as having taken the medication for 4 weeks or more.

Locations of data collection

Patients were recruited from several centres: South London and Maudsley NHS Foundation Trust; North East London Foundation Trust Eating Disorders Service; Barnet, Enfield & Haringey Mental Health NHS Trust; Oxford Health NHS Foundation Trust.

Interventions

Common features of delivery of MANTRA and SSCM

In both groups patients were offered 20 individual therapy sessions which took place once a week. In addition there were four monthly follow-up sessions. In severely underweight patients (BMI of ≤ 15 kg/m^2) sessions were extended to 30 meetings plus 4 follow-up session. In both MANTRA and SSCM, patients were offered two additional sessions with a family member or close other. Finally in both groups patients could access dietetic sessions if deemed appropriate by their clinician. In both treatments physical risk was monitored on an ongoing basis. Therapy sessions in MANTRA lasted ~ 50 minutes throughout treatment, whereas in SSCM, from the middle of treatment sessions could be briefer (i.e. about 30 minutes) in accordance with the SSCM protocol (131). This was done to ensure comparability of our study with other trials using SSCM.

MANTRA:

The MANTRA model (124) suggests that AN typically develops in people with anxious and obsessional personality traits at times of stress or increased developmental demands. Dietary restriction becomes a way of managing negative emotions and coping with stress and once established, the illness is maintained by four key maintenance factors in the cognitive,

emotional and interpersonal domains. Firstly, this includes an information processing style which is characterised by perfectionism with high standards and fear of making mistakes, excessive detail focus and poor ability to assess 'gist', and cognitive rigidity, i.e. an inability to switch between tasks or task demands. Secondly, there are impairments in emotion generation and regulation (intense emotions, lack of emotional clarity, avoidance and suppression of emotions/emotion expression, reduced ability to adaptively reappraise emotional stimuli. Thirdly, together these cognitive and emotional styles give rise to AN becoming valued by the person, i.e. the person develops positive beliefs about how AN helps them in their life (132-134). Finally, the inadvertent response of family members or close others, who may be anxious, critical or hostile may contribute to illness maintenance.

A treatment workbook is given to each patient (see data supplement DS1 in Schmidt et al. (125, 135) for details). This has both core and optional chapters, thus the information contained in the manual can be tailored to the requirements of each patient. Throughout the style of therapy is that of Motivational Interviewing (136). This means the therapist draws on the patient's experience and is responsive and reflective. Based on a thorough biopsychosocial assessment an individual case formulation is developed collaboratively. This also includes a focus on the person's personality traits, strengths and supports.. Normative and ipsative feedback, e.g. about medical risk, and thinking style is given to foster discussions about and interest in change. Health behaviour change principles and techniques are used to guide individuals towards better health and recovery (137, 138). Structure, sequence, and hierarchy of treatment procedures is clearly defined. This largely depends on an individual's clinical severity and also takes into account motivation for change, medical risk, and available individual resources and supports. Family members are asked to attend sessions as necessary.

SSCM:

This treatment was designed as as a credible comparison against CBT and IPT in an RCT (126). Full details are given in McIntosh et al. (139). There is a manual for therapists (131) which contains patient handouts giving them relevant information onon topics such as the risks of commonly used weight control behaviours and the impact of starvation on body and mind. These handouts are used flexibly throughout treatment. SSCM is designed to be delivered by eating disorders experts and aims *"to mimic outpatient treatment that could be offered to individuals with AN in usual clinical practice"*. SSCM combines principles of good clinical management (emphasising care, safety and expert knowledge) and supportive

psychotherapy (emphasising warmth, acceptance, reassurance and information giving as needed).. A central feature of SSCM is the focus on the patient's underweight and abnormal eating behaviour. Patients are given practical advice on how to work on these issues and the key message to them is that if they manage to improve their nutrition their physical and emotional health will also improve. All other therapy content is ad hoc and is dependent on what the patient wishes to discuss in a particular session.

Therapists

Twenty-eight eating disorder therapists delivered the trial therapies across the four centres. Therapists were trained in MANTRA and SSCM (2 days were provided as an introduction to each treatment). Additionally further training days were offered periodically to ensure uniform delivery of treatments across centres and to protect against 'therapeutic drift'. Therapists had to deliver both treatments to minimise allegiance effects. Supervision was provided to therapists on a weekly basis by designated trained supervisors in each team. To avoid cross-therapy contamination this was delivered separately for MANTRA and SSCM. Patients were allocated to therapists based on availability. To ensure that treatments were delivered competently and as planned, audio recordings of sessions were carried out and three tapes per patient will be chosen randomly to assess treatment adherence in both groups.

For each of their patients, therapists recorded details including e.g. number, duration and content of sessions, and details of any additional treatment.

Outcomes

All outcome measures were collected at baseline, 6 months after randomisation (i.e. approximately end of weekly sessions) and 12 months after randomisation (i.e. follow-up). Treatment credibility and acceptability ratings were taken only at 6 and 12 months. Potential outcome mediator variables were also taken at 3 months (mid-treatment), and will be reported elsewhere.

Primary outcome
- Body Mass Index (kg/m^2) at 12 months.

Secondary outcomes
- Body Mass Index (kg/m^2) at 6 months.
- Eating Disorders Examination (EDE) Global Score and Subscales (140). The EDE is a semi-structured interview that has 4 subscales: dietary restraint, eating concern,

weight concern and shape concern. The global score is created from the mean of these 4 subscales. Patients who were either unwilling or unable to participate in the EDE interview, were asked instead to complete the questionnaire version of this measure (EDE-Q) . The EDE-Q has comparable psychometric properties to the EDE interview (141).

Other psychopathology:

The Depression, Anxiety and Stress Scale - 21 (DASS-21) (95), Obsessive Compulsive Inventory Revised (OCI-R) (142).

Potential mediators:

The Cognitive Flexibility Scale (143), Beliefs about Emotions Scale (144), The Emotion Regulation Questionnaire (145) and a Visual Analogue Scale (VAS) assessing Motivation and Social Support. These will be reported elsewhere.

Treatment credibility and acceptability:

Visual analogue scales (VAS) of credibility and acceptability of treatment were specifically developed for this trial.

Neurocognitive and social-cognitive measures:

- The Wisconsin Card Sorting Task (WCST) (146, 147) is a widely used measure of set-shifting i.e. it tests the ability to flexibly switch between different tasks or rules. The participant has to match stimulus cards with one of four category cards. The stimuli are multidimensional according to colour, shape and number. The matching rules change over time and the participant has to adapt to these. We used perseverative errors as the outcome.

- The Brixton Spatial Anticipation Task (148). This also assesses set shifting. Participants have to predict the movement of a blue circle across different positions, adapting their predictions according to the pattern of movement. Error rates are assessed.

- The Rey-Osterrieth Complex Figure Test (REY) (149, 150). This tests participants' central coherence, i.e. their ability to plan, organise and assemble complex information. Participants have to copy a complex figure design and are assessed on their approach to this. The more fragmented and detail focused their approach to the task the lower their score.

- Baron-Cohen's 'Reading the Mind in Film' task (RMF) (151). This assesses Theory of Mind based on 22 brief film clips. After viewing a clip the participant is required to select one of four words to describe how the protagonist is feeling in the given situationl;.

Costs and psychosocial impairment:

- The Client Services Receipt Interview (CSRI) (152). We used a self-report version of this inventory of service use. It was adapted for the present trial to cover a range of mental and physical health services, medications, impact on employment and additional personal expenditure due to the eating disorder. CSRI data will be reported elsewhere.
- The Clinical Impairment Assessment (CIA) (153). This is a questionnaire measure assessing psychosocial impairment arising from the individual's eating disorder behaviours.

Sample size

Full details of our sample size calculation, including the data and assumptions on which this is based, can be found in our protocol paper (Schmidt et al., 2013). In brief we assumed that we would need a sample size of n = 69 patients per group to have 90% power to detect a difference in mean weight gain of 2.5 kg, using an independent samples t-test with a significance level of alpha = 0.05 and correcting for 20% attrition.

Randomisation and implementation

The randomisation sequence was generated and implemented independently from the study team by the King's Clinical Trials Unit (CTU). After participant recruitment and baseline assessment, the research assessor entered patient identification and stratification details into the online CTU system. Participants were then allocated to one of the two treatments based on a restricted stratified randomisation algorithm. The strata were (1) BMI below or above 15 kg/m^2, (2) restricting or binge/purge subtype of AN and (3) previous hospitalisation in an eating disorder unit. These factors are known to affect treatment outcome and rates of potential future inpatient treatment. The stratification was implemented by minimised randomisation with a random component. The first N cases (N was not be disclosed) were allocated entirely at random to further enhance allocation concealment.

Blinding

Whilst patients and therapists were not blinded, the research assessors, were blind to treatment allocation. In order to assess whether researcher blinding was successful, they had to make a guess at the end of 12 months assessment as to which treatment they believed the person had received.

Statistical methods

The objective of the statistical analyses was the comparison of those offered MANTRA with those offered SSCM on a number of outcomes. The primary clinical outcome was BMI (kg/m^2) at 12 months after randomisation. Secondary outcomes were continuous measures at six or 12 months follow-up (see above). All statistical analyses were based on the intention-to-treat principle, thus patients were analysed in the treatment arm to which they were randomised irrespective of whether they received the allocated treatment. All analyses were carried out in Stata 12 (154).

All outcomes were analysed using linear mixed models. Full details of the analysis plan can be found elsewhere (108, 127). Outcome variables contained considerable numbers of missing values. Full details of the treatment of missing variables can be found elsewhere (108).

<div align="center">

Results

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Participant flow and recruitment

Flow of participants through the trial is shown in Figure 1. Of the 319 patients approached 142 agreed to participate in the trial. Following baseline assessments, random allocation of the 142 participants across all four study sites resulted in 72 patients in the MANTRA arm and 70 in the SSCM arm. Three patients did not receive their allocated therapy (details in Figure 1).

Treatment completion was defined at the start of the study as attending 15 or more therapy sessions, i.e. receiving more than three quarters of the weekly treatment sessions. This definition is in line with other studies' definitions of treatment adherence (126, 130). Overall 66.9% of participants were treatment completers, with 75% of MANTRA participants and 59% of SSCM participants completing treatment ($\chi^2(1) = 1.19$, $p = 0.28$).

Non-completion of treatment predicted loss to follow up at 12 months. 45.2% of non-completing participants compared to 10.5% of completers had missing primary outcome data at 12month follow up. Details of the reasons for missing data can be found in Figure 1.

All 142 participants were included in the primary outcome analysis.
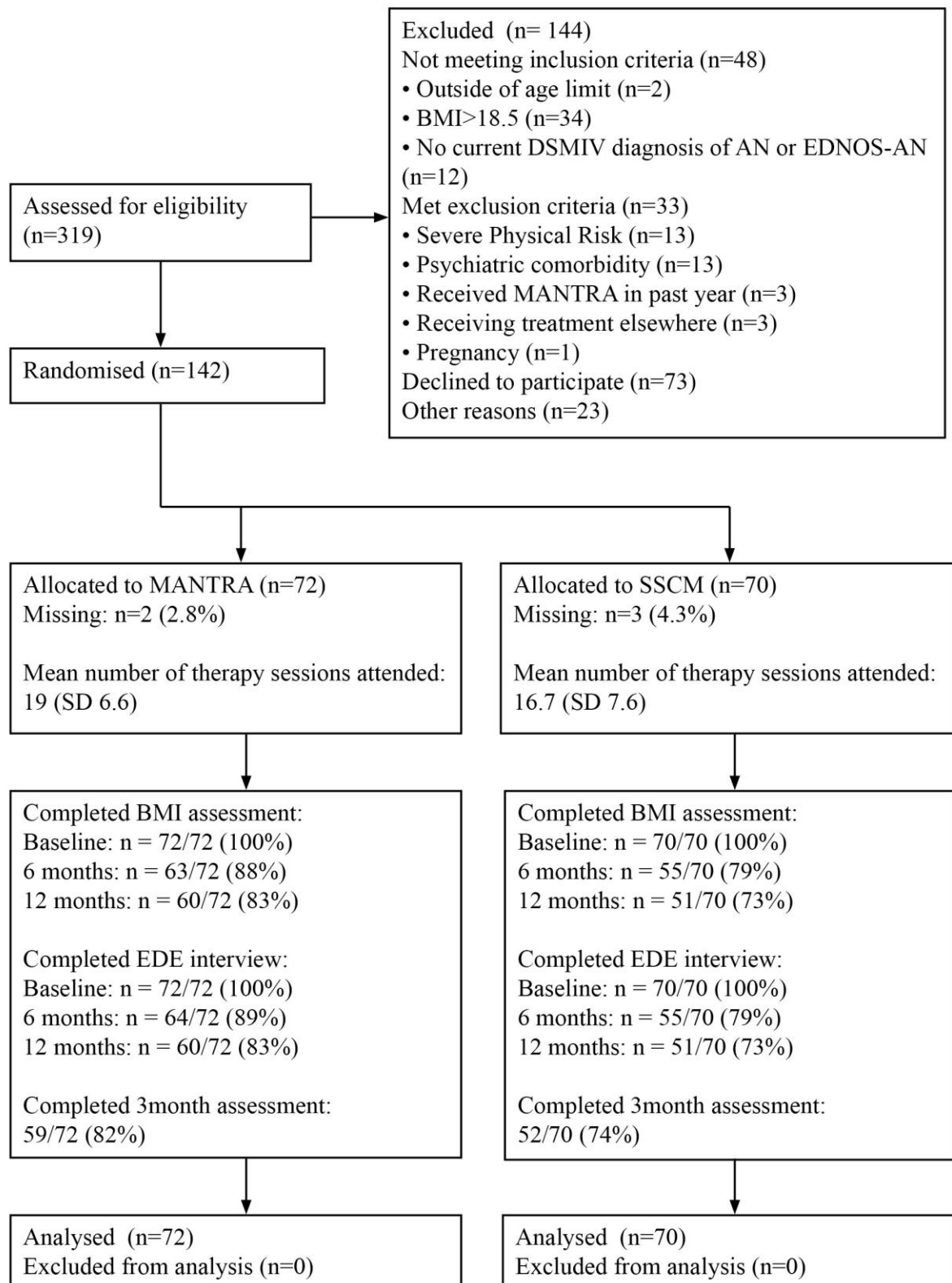
Figure 1: CONSORT flow diagram (WP2a)

The trial was conducted between June 2010 and November 2013. Between June 2010 and November 2012 participants were recruited into the trial via their initial clinical assessment with the Eating Disorders service, which was followed by a pre-intervention assessment. Delivery of the intervention occurred between June 2010 and November 2013. End of weekly treatment session follow up assessments (month 6) were completed during December 2010 to May 2013 and end of treatment follow up assessments (month 12) occurred throughout June 2011 to November 2013.

Service utilisation

Use of additional dietician sessions was not different between groups (MANTRA 33/72 (46%); SSCM 31/70 (44%)). Sixty-seven of 72 (93%) MANTRA patients and 64/70 (91.4%) SSCM patients provided information on additional service utilisation (outside the study protocol) during the study period. Eighteen of 131 patients for whom this information was available (13.7 %) had additional treatment during the study period. This was categorised into eating disorders (ED) inpatient or day-care treatment or general psychiatric inpatient treatment or other treatment. Eight of these patients had been allocated to MANTRA. Two of these had ED inpatient treatment (217 and 66 days respectively), one of these also had 30 days of ED day care treatment and one day of 'other treatment'. Three further patients only had ED day-care (175 days, 144 days and 1 day respectively). One of these also had a 10 day-inpatient alcohol detoxification programme. Two further patients had brief general psychiatric admissions (7 and 10 days respectively) because of suicidal or self-harm behaviour; one of these also had one day of 'other treatment'. One further patient had 1 day of 'other' treatment only.

Ten patients who needed additional treatment had been allocated to SSCM (15.6%). Five of these had ED inpatient care (45, 62, 110, 140 and 198 days respectively), with one of these having a second 8-day ED-admission. Three patients had ED day-care (2, 54, 183 days respectively); one of these also had a 50 days general psychiatric admission following depression and suicidal behaviour. One further patient had a 1-day general psychiatry admission followed by 11 days of home treatment and one patient had 1 day of 'other treatment. This difference was not significant. There was also no significant difference between the two treatment arms in the number of days per admission or admission days per patient.

Baseline data

Baseline characteristics of patients in both groups were comparable (Table 8) Overall the mean baseline-BMI was 16.6 (1.2) kg/m^2 and the duration of illness was 8.3 (7.3) years. Sixty-three (44.4%) patients presented with restrictive AN.

Primary outcome

Table 9 and Table 10 and show that the two treatments did not differ in their effect on BMI at 6 months ($p > 0.05$) or at 12 months ($p > 0.05$) (primary outcome).

Table 11 and Table 12 demonstrate however that there was, a significant overall effect of receiving treatment, with BMI in the total sample increasing from baseline to month 6 by 0.74 (95% CI 0.4 – 1.08) and from baseline to month 12 by 1.19 (95% CI 0.59 – 1.79).

Secondary outcomes

Table 9 and Table 10 show that the two treatments did not differ in their effect on the Global EDE score at either the 6 or 12 month time point (all $p > 0.05$).

Table 11 and Table 12 however, demonstrate that there was a significant overall effect of receiving treatment, with mean EDE Global decreasing from baseline to month 6 by 0.63 (95% CI -0.85 - -0.42) and from baseline to month 12 by 0.84 (95% CI -1.08 – 10.59)

Table 9 and Table 10 show that there was no difference between the two treatments at 6 or 12 month follow up for all other secondary outcomes (all p>0.05).

Again, Table 11 and Table 12 demonstrate that there was a significant overall effect of receiving treatment for all EDE subscales, DASS-21, CIA, WCST and Brixton scores after month 6 (all $p < .01$), whereas OCI-R REY and RMF did not change significantly (all $p > .05$).

At month 12 there was a significant overall effect of treatment for all EDE subscales, DASS-21, CIA, Brixton and REY scores (all $p < .01$), whereas OCI-R, WCST and RMF did not change significantly (all $p > .05$).

Table 8: Demographic and Clinical Characteristics at Baseline

	Whole group		MANTRA		SSCM	
	n		n		n	
Demographic details						
Age at randomisation, years: mean (*SD*)	142	26.7 (7.7)	72	27.5 (8.1)	70	25.9 (7.1)
Male:Female, *n*	142	3:139	72	0:72	70	3:67
Years in Education, mean (*SD*)	125	15.8 (2.3)	63	16.1 (2.1)	62	15.5 (2.5)
Has a partner, *n* (%)	138	50 (35.2)	72	21 (29.2)	66	29 (41.4)
Clinical details						
Diagnosis, *n* (%)	142		72		70	
AN-R		63 (44.4)		35 (48.6)		28 (40.0)
AN-BP		44 (31.0)		22 (30.6)		22 (31.4)
EDNOS		35 (24.7)		15 (20.8)		20 (28.6)
BMI, kg/m^2, mean (*SD*)	142	16.64(1.2)	72	16.61 (1.2)	70	16.62 (1.3)
Weight, kg, mean (*SD*)	142	45.1 (4.9)	72	44.8 (4.5)	70	45.4 (5.4)
Age at onset, years, mean (*SD*)	132	17.7 (6.5)	67	17.3 (6.5)	65	18.1 (6.6)
Illness duration, years, mean (*SD*)	134	8.3 (7.3)	67	9.3 (7.9)	67	7.2 (6.5)
Previous eating disorder treatment, *n* (%)	140	80 (56.3)	70	41 (56.9)	70	39 (55.7)
EDE, mean (*SD*)	142	3.3 (1.3)	72	3.1 (1.3)	70	3.5 (1.3)
DASS21, mean (*SD*)	138	30.5 (12.7)	69	29.6 (11.5)	69	31.4 (13.8)
CIA, mean (*SD*)	141	32.6 (8.9)	71	32.1 (9.0)	70	33.0 (8.9)
Current antidepressant medication, *n* (%)	140	55 (38.7)	70	29 (40.3)	70	26 (37.1)

MANTRA, Maudsley Model of Anorexia Nervosa Treatment for Adults; SSCM, Specialist Supportive Clinical Management; AN-R, anorexia nervosa restricting type; AN-BP, anorexia nervosa binge eating/purging type; EDNOS, eating disorder not otherwise specified; BMI, body mass index; EDE, eating disorder examination; DASS21, depression anxiety stress scale; CIA, clinical impairment assessment.

This table is reproduced from: Schmidt, U., Magill, N., Renwick, B., Keyes, A., Kenyon, M., Dejong, H., . . . Yasin, H. (2015). The Maudsley Outpatient Study of Treatments for Anorexia Nervosa and Related Conditions (MOSAIC): Comparison of the Maudsley Model of Anorexia Nervosa Treatment for Adults (MANTRA) With Specialist Supportive Clinical Management (SSCM) in Outpatients With Broadly Defined Anorexia Nervosa: A Randomized Controlled Trial. Journal of Consulting and Clinical Psychology, epub ahead of print.

Table 9: MANTRA vs SSCM -Estimated treatment effects at 6 months post-randomisation

	Predicted mean (s.e.), baseline fixed to sample average					
	MANTRA	SSCM	Est. group difference‡	Test	95% CI ‡	Standardised coefficient‡
BMI (kg / m^2)^P	17.52 (0.21)	17.24 (0.23)	0.28	$t = 0.91$, $p = 0.36$	-0.32, 0.88	0.23
EDE Global	2.72 (0.14)	2.63 (0.15)	0.09	$t = 0.48$, $p = 0.63$	-0.29, 0.48	0.07
EDE Restraint	2.48 (0.29)	2.43 (0.30)	0.05	$t = 0.13$, $p = 0.90$	-0.68, 0.78	0.03
EDE Eating Concern	2.27 (0.16)	2.28 (0.18)	-0.01	$t = -0.05$, $p = 0.96$	-0.47, 0.45	-0.01
EDE Shape Concern	3.16 (0.18)	2.01 (0.20)	0.14s	$t = 0.55$, $p = 0.58$	-0.37, 0.65	0.08
EDE Weight Concern	2.74 (0.19)	2.68 (0.21)	0.07	$t = 0.24$, $p = 0.81$	-0.48, 0.61	0.04
DASS-21	27.12 (1.54)	27.25 (1.62)	-0.12	$t = -0.06$, $p = 0.96$	-4.50, 4.25	-0.01
OCI-R	23.01 (1.86)	21.58 (1.97)	1.42	$t = 0.58$, $p = 0.56$	-3.41, 6.26	0.10
CIA	26.96 (1.58)	26.93 (1.69)	0.03	$t = 0.01$, $p = 0.99$	-4.25, 4.31	<0.01
Wisconsin Card Sorting Task	1.74 (0.13)	1.58 (0.20)	0.15	$t = 0.69$, $p = 0.49$	-0.29, 0.60	0.21
Brixton	10.49 (0.65)	10.24 (0.79)	0.25	$t = 0.30$, $p = 0.77$	-1.43, 1.94	0.04
REY	1.36 (0.04)	1.31 (0.05)	0.05	$t = 0.72$, $p = 0.48$	-0.08, 0.17	0.18
Reading the Mind in Films	13.91 (0.45)	13.08 (0.48)	0.84	$t = 1.38$, $p = 0.17$	-0.35, 2.02	0.30

‡ coefficients represent estimated treatment effect of MANTRA – SSCM

MANTRA, Maudsley Model of Anorexia Nervosa Treatment for Adults; SSCM, Specialist Supportive Clinical Management; BMI, body mass index; EDE, eating disorder examination; DASS-21, depression anxiety stress; OCI-R, Obsessive Compulsive Inventory Revised; scale; CIA, clinical impairment assessment; REY CC, Rey-Osterrieth Complex Figure Test.

Table 10: MANTRA vs. SSCM - Estimated treatment effects () at 12 months post-randomisation

	Predicted mean (s.e.), baseline fixed to sample average					
	MANTRA	SSCM	Estimated group difference‡	Test	95% confidence interval‡	Standardised coefficient‡
BMI (kg / m²)^P	18.04 (0.32)	17.72 (0.35)	0.31	$t = 0.67$, $p = 0.50$	-0.60, 1.22	0.25
EDE Global	2.37 (0.16)	2.58 (0.17)	-0.22	$t = -0.95$, $p = 0.34$	-0.66, 0.23	-0.17
EDE Restraint	2.49 (0.22)	2.67 (0.24)	-0.18	$t = -0.55$, $p = 0.58$	-0.82, 0.46	-0.12
EDE Eating Concern	1.82 (0.18)	2.17 (0.20)	-0.35	$t = -1.33$, $p = 0.18$	-0.87, 0.17	-0.25
EDE Shape Concern	2.83 (0.18)	2.89 (0.19)	-0.06	$t = -0.24$, $p = 0.81$	-0.57, 0.44	-0.04
EDE Weight Concern	2.32 (0.20)	2.61 (0.22)	-0.29	$t = -1.00$, $p = 0.32$	-0.86, 0.28	-0.18
DASS-21	26.00 (1.54)	25.16 (1.70)	0.84	$t = 0.37$, $p = 0.72$	-3.69, 5.37	0.07
OCI-R	22.01 (1.96)	20.81 (2.10)	1.20	$t = 0.46$, $p = 0.64$	-3.87, 6.28	0.09
CIA	23.56 (1.57)	24.62 (1.82)	-1.06	$t = -0.42$, $p = 0.67$	-6.00, 3.89	-0.12
Wisconsin Card Sorting Task	1.82 (0.13)	1.83 (0.20)	-0.01	$t = -0.05$, $p = 0.96$	-0.44, 0.42	-0.01
Brixton	9.34 (1.71)	5.87 (2.13)	3.47	$t = 1.41$, $p = 0.16$	-1.39, 8.33	0.60
REY	1.43 (0.05)	1.39 (0.07)	0.03	$t = 0.42$, $p = 0.68$	-0.12, 0.18	0.11
Reading the Mind in Films task	13.88 (0.68)	13.39 (0.65)	0.49	$t = 0.63$, $p = 0.53$	-1.05, 2.02	0.18

‡ coefficients represent estimated treatment effect of MANTRA – SSCM.

MANTRA, Maudsley Model of Anorexia Nervosa Treatment for Adults; SSCM, Specialist Supportive Clinical Management; BMI, body mass index; EDE, eating disorder examination; DASS-21, depression anxiety stress; OCI-R, Obsessive Compulsive Inventory Revised; scale; CIA, clinical impairment assessment; REY CC, Rey-Osterrieth Complex Figure Test.

Table 11: Estimated change in mean outcome between baseline and month 6 (average of both treatment arms)

Outcome	Estimated change	Standard error	Test	95% CI
BMI (kg / m^2)^P	0.74	0.17	$t = 4.31$, p < 0.001	0.40, 1.08
EDE Global	-0.63	0.11	$t = -5.80$, p < 0.001	-0.85, -0.42
EDE Restraint	-1.30	0.24	$t = -0.13$, p < 0.001	-1.77, -0.83
EDE Eating Concern	-0.57	0.14	$t = -4.10$, p < 0.001	-0.84, -0.30
EDE Shape Concern	-0.41	0.15	$t = -2.65$, p < 0.01	-0.71, -0.11
EDE Weight Concern	-0.45	0.15	$t = -2.94$, p < 0.01	-0.74, -0.15
DASS-21	-3.38	1.14	$t = -2.97$, p < 0.01	-5.62, -1.14
OCI-R	-0.90	1.62	$t = -0.55$, p $= 0.58$	-4.12, 2.32
CIA	-5.41	1.43	$t = -3.79$, p < 0.001	-8.23, -2.59
Wisconsin Card Sorting Task	-0.36	0.13	$t = -2.84$, p < 0.01	-0.61, -0.11
Brixton	-2.02	0.50	$t = -4.02$, p < 0.001	-3.02, -1.03
REY	0.05	0.04	$t = 1.43$, p $= 0.15$	-0.02, 0.13
Reading the Mind in Films	0.52	0.36	$t = 1.46$, p $= 0.15$	-0.18, 1.22

MANTRA, Maudsley Model of Anorexia Nervosa Treatment for Adults; SSCM, Specialist Supportive Clinical Management; BMI, body mass index; EDE, eating disorder examination; DASS-21, depression anxiety stress; OCI-R, Obsessive Compulsive Inventory Revised; scale; CIA, clinical impairment assessment; REY CC, Rey-Osterrieth Complex Figure Test.

Table 12: Estimated change in mean outcome between baseline and month 12 (average of both treatment arms)

Outcome	Estimated change	Standard error	Test	95% CI
BMI (kg / m^2)^P	1.19	0.30	$t = 3.91$, $p < 0.001$	0.59, 1.79
EDE Global	-0.84	0.12	$t = -6.78$, $p < 0.001$	-1.08, -0.59
EDE Restraint	-1.16	0.17	$t = -6.81$, $p < 0.001$	-1.49, -0.82
EDE Eating Concern	-0.85	0.17	$t = -5.05$, $p < 0.001$	-1.18, -0.52
EDE Shape Concern	-0.64	0.14	$t = -4.55$, $p < 0.001$	-0.92, -0.37
EDE Weight Concern	-0.70	0.17	$t = -4.09$, $p < 0.001$	-1.04, -0.36
DASS-21	-5.02	1.18	$t = -4.25$, $p < 0.001$	-7.34, -2.70
OCI-R	-1.59	1.88	$t = -0.85$, $p = 0.40$	-5.31, 2.13
CIA	-8.56	1.18	$t = -7.28$, $p < 0.001$	-10.87, -6.25
Wisconsin Card Sorting Task	-0.23	0.13	$t = -1.74$, $p = 0.09$	-0.49, 0.03
Brixton	-4.42	1.59	$t = -2.78$, $p < 0.01$	-7.58, -1.27
REY	0.12	0.05	$t = 2.40$, $p = 0.02$	0.02, 0.23
Reading the Mind in Films	0.64	0.55	$t = 1.16$, $p = 0.25$	-0.46, 1.74

MANTRA, Maudsley Model of Anorexia Nervosa Treatment for Adults; SSCM, Specialist Supportive Clinical Management; BMI, body mass index; EDE, eating disorder examination; DASS-21, depression anxiety stress; OCI-R, Obsessive Compulsive Inventory Revised; scale; CIA, clinical impairment assessment; REY CC, Rey-Osterrieth Complex Figure Test.

Recovery rates

At 12 month follow up participants were split into 3 groups, recovered, partially recovered and not recovered. These were defined as (a) recovered: BMI>18.5 kg/m^2 and EDE Global Score <2.77. (b) partially recovered: BMI<17.5 kg/m^2 and EDE Global Score <2.77, BMI>17.7 kg/m^2 & ≤18.5 kg/m^2 or BMI>18.5 kg/m^2 and EDE Global Score >2.77. (c) not recovered: BMI≤ 17.5 kg/m^2 and EDE Global Score >2.77.

Proportions of participants falling into these categories at 12 months were as follows: MANTRA: recovered 13/72 (18.1%), partially recovered 36/72 (50%) and not recovered 9/72 (12.5%). SSCM: recovered 8/70 (11.4%), partially recovered 32/70 (45.7) and not recovered 9/70 (12.9%). There was no association between treatment allocation and recovery (χ^2(3) = 2.80, p = 0.42).

Baseline BMI as a potential moderator of primary and secondary outcomes

We also examined whether baseline BMI was a potential moderator of treatment effect on BMI at 6 and 12 months, dividing participants into those with a baseline BMI of < 17.5 kg/m^2, (77% of MANTRA and 70% of SSCM participants) and those with a BMI of > 17.5 kg/m^2 (18.1% of MANTRA and 25.7% of SSCM participants). (This information was missing for 4.2% and 4.3% of participants in MANTRA and SSCM groups respectively)

There was no evidence of a statistically significant interaction between treatment group and whether baseline BMI was above or below 17.5kg/m^2 when BMI was the outcome. However, on visual inspection of the estimated effects, it does appear that the effect of treatment (favouring MANTRA) was larger amongst those with lower baseline BMI (see Table 13).

Baseline BMI was also investigated as a potential moderator of secondary outcomes. No evidence of a statistically significant interaction between treatment group and whether baseline BMI was more or less than 17.5kg/m^2 was found for these other outcomes.

Harms

One SSCM patient died. No other harms were noted.

Table 13: Estimated effects of treatment on BMI at the different levels of baseline BMI (whether less than or more than 17.5kg/m^2)

Variable	Level	Estimated group difference‡	t score	p-value
	6 months after randomisation			
Baseline BMI	≤17.5kg/m^2	0.41	1.32	0.19
	>17.5kg/m^2	-0.04	-0.07	0.94
	12 months after randomisation			
Baseline BMI	≤17.5kg/m^2	0.55	1.26	0.21
	>17.5kg/m^2	-0.08	-0.10	0.92

‡ coefficients represent estimated treatment effect of MANTRA – SSCM

Treatment acceptability and credibility

There were no significant difference in acceptability and credibility ratings between MANTRA and SSCM at 6 months (Acceptability: M = 8.5 (2.0), S = 8.0 (2.2) [$t(100) = 1.33$, $p = .18$] Credibility: M = 6.4 (3.1), S = 5.8 (2.7) [$t(100) = 1.1$, $p = .29$]). However, at 12 month MANTRA was given significantly higher ratings on both actability and credibility compared to SSCM (Acceptability: M = 8.6 (1.8), S = 7.8 (2.3) [$t(91) = 2.01$, $p < 0.05$] Credibility: M = 6.8 (3.1), S = 5.5 (2.7) [$t(91) = 2.24$, $p < 0.05$]).

<div align="center">

Discussion

</div>

Main findings

Firstly, overall participants showed significant improvements in terms of BMI, eating disorder symptoms, depression, anxiety and stress and psychosocial impairment after 6 months of weekly treatment sessions. These improvements were either maintained at twelve months post-randomisation or got larger. Secondly, there were no differential effects between the two treatments in terms of primary and secondary outcomes and further service utilisation. Therefore our main hypotheses were not confirmed. However, BMI, EDE and proportions of recovered participants all somewhat favour MANTRA at 12 months and exploratory moderator analysis suggested that especially in the patients who were more severely ill at baseline the treatment effect in relation to BMI (favouring MANTRA) got (non-significantly) larger at 12 months.

There was a mixed picture of results in terms of neuro- and social-cognitive performance. There was no effect of treatment on social cognition, however, participants were not particularly impaired on this task at baseline (155) so this lack of improvement is unsurprising. Central coherence and cognitive flexibility as measured by the Brixton Spatial Anticipation Task improved significantly by month 12; however cognitive flexibility as measured by the WCST did not, but again participants were not particularly impaired at baseline (15).

Comparison of main findings with those of other trials

The degree of BMI change observed in the MOSAIC Trial is comparable to that found in our earlier single centre pilot RCT (total n = 72) which used identical study inclusion criteria and which also compared MANTRA and SSCM (135), suggesting that these treatments can be disseminated to other UK centres with relatively brief initial training (2 days) of therapists and booster training (1 day).

Comparison against other trials needs to be approached cautiously because of differences in patient populations. Perhaps the findings from the present study can be compared most easily against the large German psychotherapy trial by Zipfel et al (130) which compared focal psychodynamic therapy, CBT and optimised treatment as usual in outpatients with AN. Patients in this trial had comparable baseline BMIs (between 16.6 and 16.8 kgs/m^2) but received a somewhat higher 'dose' of psychotherapy (40 sessions over 10 months). Patients were followed up at 13 months post-randomisation and at 22 months post-randomisation. 13-months BMI outcomes in the Zipfel et al (130) study were between 17.6 kgs/m^2 (focal psychodynamic therapy) and 17.4 kgs/m^2 (CBT and Optimised TAU) whereas our 12-month BMI outcomes were 18.0 kgs/m^2 in MANTRA and 17.7 kgs/m^2 in SSCM. Thus our BMI improvements stand up well in this international comparison.

Two other previous trials have used SSCM (126, 156). Comparison of our data against these trials is difficult. One of these trials had patients who had a significantly milder form of AN (baseline mean BMI 17.3 kgs/m^2) (126) and the other specifically focused on chronic patients (with a mean illness duration of 15.5 and 17.7 years for CBT and SSCM respectively (156). In the McIntosh study, SSCM BMI outcomes were superior to CBT and IPT BMI outcomes at end of treatment but not at long-term follow-up (157). In the Touyz et al (156) study at 12-month follow-up BMI gains were modest (0.5 kgs/m^2) and identical for both groups.

Other findings

Service utilisation

There was no difference in terms of further service utilisation between the two treatments. This is in contrast to findings from our pilot trial which also compared SSCM with MANTRA (135) and where all cases of hospital admissions and day-care treatment were in the MANTRA group. However, in our earlier smaller trial there was an imbalance between the two groups at baseline, with a significantly higher proportion of SSCM compared to MANTRA participants having a partner (and therefore being in a prognostically better group). This may explain the differences between the two treatments in service utilisation in this earlier trial and suggests the previously observed difference was a feature of the pilot sample rather than an inadequacy in the MANTRA treatment.

Trial retention, treatment completion and acceptability

Participant retention in the trial was very good with 83% and 73% of MANTRA and SSCM participants respectively providing BMI and EDE data at 12 months. In comparison in the trial by Zipfel and colleagues (130) at 13 month assessment between 58.5% (optimised TAU) and 82.5% (CBT) participants provided data.

Treatment completion rates also compare well against those of other studies that used a similar definition of treatment completion. 75% of MANTRA and 59% of SSCM patients completed treatment. In the McIntosh et a. (126) trial 62.5% of participants completed treatment and in the Zipfel et al (130) trial 66% and 81.3% of focal psychodynamic therapy and CBT participants completed treatment.

Finally and of note, there was a significant difference between treatment acceptability and credibility ratings at month 12, with MANTRA being rated more favourable on both compared to SSCM. This may be because MANTRA is a manual based treatment where patients continue to have access to key resources during the course of therapy and beyond. The benefits the manual may become more apparent following the end of weekly sessions, leading to a more positive longer term experience.

Harms

One SSCM patient died during the study. This patient had very severe and chronic AN. It has been documented in many studies that chronically ill, low-weight AN patients such as the one in our study do have a highly elevated mortality risk (e.g. 67). The causes of death typically

are related directly to consequences or complications of the illness (via malnutrition or abnormal weight control methods) and this is thought to be the case here. Previous trials of AN outpatient treatment in adults have reported deaths. For example, in a trial by Dare et al. (33) one patient out of 84 died over the course of the trial and in the study by McIntosh et al. (158) there was one death amongst 56 participants.

Patient and therapist experience of MANTRA and SSCM

The present trial is the only RCT of treatments for AN so far to include qualitative feedback from patients and therapists which we published separately prior to the outcome evaluation, as is recommended for such process evaluations (159-161). In particular, process data from therapists, who of course were able to compare and contrast these treatments, identified marked differences between these two treatments, in terms of the therapy focus, therapeutic strategies and applicability to a wide range of patients (160). Process data from patients largely agree with these findings, and in addition strongly point to the quality of the therapeutic relationship, as the basis for a successful therapy (159). Both treatments were perceived as having strengths and weaknesses. A further process evaluation examined written qualitative feedback from all study participants at 12 months (161). 82 study participants provided such written feedback, significantly more from the MANTRA group than the SSCM group. MANTRA patients also tended to write in more detail and give more positive feedback when compared to individuals receiving SSCM. Taken together with quantitative acceptability and credibility ratings these process evaluation findings suggest that patients prefer MANTRA and therapists like it too. It thus provides a good alternative to SSCM. Of note, the greater acceptability of MANTRA may mean that patients are more willing to have further treatment if required or have better outcomes in the longer term. Assessment of these long-term effects of MANTRA and SSCM is currently under way.

Strengths

The strengths of the present study include that it is the largest RCT of first line psychological treatments for adults outpatients with AN to be carried within the UK and the second largest in the world (see 130). The study had good participation rates at follow-up data points, good treatment completion, and high acceptability and good outcomes compared to other studies. As such the MOSAIC trial improves our limited evidence-base regarding outpatient treatments in this hard-to-treat population. This study is also novel in that it is the first AN

trial to incorporate both qualitative and quantitative measures of the therapeutic process and therefore offers a greater insight into patient and therapist perceptions of the two treatments.

Limitations

The MOSAIC Trial also had limitations. Firstly, although the trial is the largest ever to be carried out within the UK it is still not large enough to perform conclusive mediation and moderation analyses of the core illness maintenance factors which MANTRA attempts to ttarge. However, we will be able to amalgamate the data from the present trial with the data from our earlier smaller RCT (135) which used an identical design and overlapping assessments to allow more definitive moderator and mediator analyses. The combined sample size from both these trials will be 214 patients.

Secondly although the 'lost to follow up' rate within our overall sample was acceptable, the rate for participants assigned to SSCM is 10% greater than those receiving MANTRA. Therefore, information on recovery in individuals in this group is more limited.

Finally, we were restricted by funding to a relatively short-term follow-up of 12 months. Further (2 year) follow up is necessary to measure the longer term effects of these two treatments on primary and secondary outcomes.

Generalisability

The MOSAIC Trial included four specialist eating disorder services and the interventions were delivered by a large number and broad range of therapeutic staff, with different professional backgrounds and different degrees of experience, so the study can be seen to reflect usual clinical practice. The trial also had very few exclusion criteria, making the sample as generalisable as possible and leading to the inclusion of a sample with a very broad range of clinical severity and BMI. As in usual clinical practice, trial therapists were able to conduct both treatments. Through therapist interviews (160) we have been able to confirm that both treatments were experienced very differently and delivered with fidelity. Further confirmation of this will be reported separately through analysis of the therapeutic session recordings.

Conclusions and future outlook

The significant improvement of patients in both groups suggests that both these two very different treatments have value as first line outpatient treatments for adults with AN. In the

original trial from New Zealand in which SSCM was first used (126), SSCM was found to outperform two active treatments (CBT and interpersonal therapy) against the investigators' hypothesis, and therefore provides a very high standard of control treatment. Comparable weight gain and comparable reductions in eating disorder psychopathology between MANTRA and SSCM are therefore encouraging.

The current report includes an intention-to-treat analysis only. In future, we will also conduct a completer analysis, an analysis of health economic outcomes and of cost and cost-effectiveness and an exploratory analysis of potential treatment mediators. Finally we will also conduct analyses of session recordings to assess treatment fidelity and therapeutic process. We are in the process of completing a 2-year follow-up of the MOSAIC patients, given preliminary evidence from the long-term follow-up of the New Zealand study that SSCM effects may become less effective over the longer term (157).

Chapter 5. Cognitive Remediation and Emotional Skills Training (CREST) for Inpatients with Anorexia Nervosa (WP2b)

Kate Tchanturia, Helen Davies, Helen Sharpe & Ulrike Schmidt

Abstract

Word count: 199

Objectives: To evaluate the benefits of Cognitive Remediation and Emotional Skills Training (CREST) for patients with anorexia nervosa (AN) receiving inpatient treatment.

Design: This project/chapter has three studies: 1) case report; 2) qualitative study of service users' views about CREST; 3) quasi-experimental comparison of CREST and treatment as usual (TAU) in two inpatient settings.

Participants: Adult inpatients with AN.

Interventions: The main novel intervention used in this project is CREST, which consists of simple cognitive exercises and simple emotion regulation, recognition and processing skills training, promoting micro skills in social communication and self-regulation as well as facilitating better self-awareness.

Main outcome measures: Outcomes included qualitative feedback and neuropsychological tests targeting flexibility of thinking, central coherence and theory of mind. Clinical outcomes (BMI, EDEQ) were also reported.

Results: Qualitative assessments demonstrated CREST to be acceptable and perceived as beneficial by patients. Additionally, self-report questionnaires demonstrated improvements; however, quantitative data were less promising, showing no clear differences between the CREST and TAU groups in terms of cognitive or clinical outcomes.

Conclusions: Future work will focus on revisions to the CREST manual based on the outcomes of this work, as well as greater refinement of the measures used in subsequent quantitative evaluations.

Introduction

Inpatient treatment in the majority of countries is reserved for the most severe patients with anorexia nervosa (AN). NICE guidelines (NICE 2004) encourage treatment innovations for the severely ill eating disordered patient population.

One of the empirically supported models of AN (19) suggests inefficiencies in cognitive style and difficulties in emotion generation and regulation as factors maintaining the illness ((14, 16, 111, 162, 163). A related division is that into 'cold' cognition which is based on logic and rational thinking, whereas 'hot' cognition is based on feeling, intuition, emotional response and motivation (164). Targeting cognitive styles ('cold' cognition) has been found to be an effective adjunct in treatment of inpatients, using the Cognitive Remediation Treatment which improves neuropsychological task performance improved.

The aim of these three studies was to test a novel intervention which targets 'cold' and 'hot' cognition in a manualised individual format for inpatients. CREST is a brief (1 hour, 10 sessions) psychological intervention. It focuses on inflexible and detail-focused thinking styles (2 sessions), and additionally focuses on learning to recognise emotions , the management and expression of emotions, and recognising and acknowledging positive emotions (8 sessions). A range of psychoeducational modules and interactive tasks within CREST have been developed to facilitate individuals to: a) learn about the adaptive function of emotions, b) learn how to identify emotions, c) and, d) practice experiencing and expressing emotions.

Study 1: Case study

Setting and referral

Anna is a 21 year-old Caucasian British woman informally admitted to the Eating Disorder Unit with Anorexia Nervosa (AN) and self-harming behaviour.

Assessment

On admission, Anna had a Body Mass Index (BMI) of 13.1 kg/m^2 (the healthy weight ranges between 19-25 kg/m^2). She fulfilled diagnostic criteria for the restricting subtype of AN. She was significantly restricting her diet and exercising excessively prior to her admission, which

led to significant weight loss. She also described a number of rigid rules and ritualistic behaviours surrounding her eating, and would become distressed if her routines were disrupted. Anna had a distorted body image and body dissatisfaction, and described herself as 'disgusting' and 'fat', despite being objectively emaciated. She seemed to lack a sense of personal identity, but felt that AN gave her an identity and a sense of specialness. She rated the importance of change as 2/10, and her perceived ability to change as 2/10.

Prior to her admission Anna was frequently engaging in self-harm including punching, scratching, and burning herself (superficially) on her arms and hands. She described using these behaviours as a means of managing adverse emotional states. She did not have any current suicidal ideation and denied plans to take her own life.

Anna reported growing up in an emotionally invalidating environment, where her feelings and thoughts were often marginalised by her parents, and she felt that she was 'second best' to her younger brother.

Key triggers for Anna's eating disorder appeared to be her failing her GCSE exams and being bullied by her peers who told her she was not 'good enough' for her boyfriend. These events seem to activate and reinforce negative core-beliefs that Anna had about herself. Anorexia may have provided Anna with a sense of achievement and specialness, at a time when she was feeling like a failure in other domains. AN and her subsequent self-harm also gave her a way of managing her emotions, which she found confusing and aversive.

Intervention

Anna was offered Cognitive Remediation and Emotional Skills Training (CREST) over 10 individual sessions. This was deemed to be a particularly useful treatment option for Anna, given her difficulties in managing her emotions. Anna's mother also attended a series of family meetings with Anna in which they were supported to gain insight into each other's perspectives. These sessions also helped in supporting Anna's mother in her own struggle to support Anna.

Outcomes

Anna did not complete the outcome measures given pre- and post- CREST. However, over the course of her 14 week admission her weight did increase to a BMI of 14.7 kg/m^2. Her self-reported rating of the importance of change rose from 2/10 to 5/10, and her perceived ability to change also rose from 2/10 to 5/10. Anna reported that she found the intervention

(CREST and family work) very useful in helping her to reduce her self-harming and in managing her emotions, as well as allowing for a change in the relationship with her mum to develop. Anna's mother also said that she found the CREST work very helpful and felt more confident in her ability to support Anna in her recovery.

Study 2: Qualitative evaluation

Aims

The aim of this study was to explore patients' views and experience of individual CREST.

Methods

Participants

Twenty-eight patients in the National Adult Eating Disorder Inpatient Service completed CREST and were included in this study. All participants had a DSM-IV (165) diagnosis of AN established by an experienced clinician. Participants mean age was 25 (range 13–40). The mean BMI before starting CREST was 14.7 (range 11.5-18.1). Eleven patients did not complete all sessions and were excluded from this study. Four patients were discharged from the hospital before they had completed CREST and seven disengaged from the inpatient treatment programme.

Data collection

All patients completed an end of therapy reflection form following CREST. This study was reported in detail by Money and colleagues (2011) and the main idea was to assess patients' reflections on the helpful aspects of therapy and the points for improvement. Responses were anonymised and then transcribed. All participants were given information about the study and consented to participation.

Analysis

The participants' qualitative feedback was rated by two independent researchers. Each question was analysed based on the methods described in Elo and Kyngas (166), and Joffe and Yardley (167). Initially the two researchers searched the data independently for codes or instances, thereafter they met to agree on how these could be grouped together to form different categories. The main categories were however predetermined by the questions asked.

Results

Detailed results tables were reported in the publication by Money and colleagues (2011), in which patient responses indicated benefits from the therapy and directions for improvement. In this chapter we will illustrate what the patients had to say about CREST with quotes.

In the table below (Table 14) we have provided a few illustrations of what patients had to say about the most helpful aspects of CREST and what we could improve in the future:

Table 14: End of therapy reflection

Were there any aspects that were especially helpful?
"Finding out that emotions are telling you that you need something - now when I feel upset I look at what needs to be done about it instead of limiting my food intake."
"Learning to identify emotions within myself. Learning a means of communicating these emotions. Realising that I have rights and that emotions are not 'good' or 'bad', they just tell me something about what I need."
"Speaking to psychologists."
"Really learning that all feelings are welcome and ok. Learning how to express myself. Putting names to feelings."
"I found it useful being in surroundings where you could see the illness in people and you just want to recover so badly."
"Identifying emotions and needs."
"Set times to talk about emotions. Focusing on positive emotions and not being upset when things go wrong.""The calm, relaxed environment. The way that the therapies can link into everyday experiences. The visual activities."
"I found that attempting to identify emotion through body language, facial expression in others, and as a colour/sound/animal helped me to understand my own feelings a little more. Showing me that a negative emotion, i.e. anger, can be a positive thing as it can incite change, helped also."
"The detail to different types of emotions and also all the challenges and homework

that I had to complete. I found these really identified and elicited all the factors I need to work on."

"Everything, talking about different emotions, realising how I deal with my emotions and learning how to express my emotions more instead of bottling them up."

What do you think could be improved?

"Stop making me eat!"

"More sessions."

"Longer course."

"Proper psychological therapy, support on the unit, being able to talk to someone daily, not being kept waiting and having to wait all day if necessary just to see someone to answer a question."

"Less basic work at the start. A few more sessions."

"Possibly a few more sessions. More about identifying and handling different emotions."

"Generic idea, hard to improve when ultimately cross-section research that is not personal."

"I felt a few more sessions may have been beneficial to me with a bit more focus on different specific emotions. But on the whole both the content and facilitation of the therapy was a good, helpful experience."

"I feel another set of CREST should be administered after 1:1 psychology is happening with patients. The purpose would be to look at emotions in a different and more in-depth way."

"No, as I found the sessions helpful."

Discussion

The main aim of the qualitative study was to evaluate the acceptability of the CREST intervention for inpatients with AN. In the national inpatient ward where this study took place, the majority of the patients are nutritionally compromised (according to our annual audit data the mean BMI at admission is 13.00). In a severely ill AN patient, treatment engagement and meaningful psychological intervention delivery is challenging. Research shows that acutely ill AN patients have a major difficulty in correctly identifying and expressing emotions (16, 162, 168, 169). CREST includes information about basic emotion processing skills and aims to give patients simple tools and strategies to notice their own emotions and express their needs in a safe way. Alongside enhancing these skills, CREST also had a benefit in terms of increasing assertiveness. Many of the patients who received this intervention reported that CREST was helpful and the strategies they learnt will be useful in the future. This highlights an improvement in patients' confidence and perceived ability to express thoughts and emotions. From the qualitative outcome analysis we could also conclude that CREST has a positive impact on reducing inter-personal problems known to be present in this population (19, 170).

Using qualitative outcomes from the study and learning from patients' personal experiences were very useful steps in terms of gathering evidence for CREST.

Limitations

This qualitative study had some clear limitations, for example, feedback was not obtained from patients who dropped out of the treatment. There is also the possibility that patients wanted to please clinical and research staff with positive comments, therefore in the future independent evaluation after discharge from the ward programme might provide more objective data.

A further limitation was that the study was conducted on one inpatient programme only. Future studies may consider evaluating CREST across multiple sites to explore its generalisability.

From the individual work and analysis of the quotes we have obtained very useful ideas about how to help patients to implement some of their new skills in real life. Qualitative feedback from the individual format of CREST led to the idea of developing a group protocol. This allows patients to practice and role-play the skills worked on in the individual sessions and express their needs and feelings in the group.

Study 3: Controlled trial

Aims

The aims of this study were to use cognitive (neuropsychological) assessments to: 1) investigate changes in performance on cognitive flexibility, central coherence and emotion processing tasks in inpatients with AN following CREST, and, 2) investigate the magnitude of the changes on a cognitive and emotion test battery used in the study with patients who have received CREST plus treatment as usual (TAU) (referred to from now on as the CREST group) compared to patients who have received TAU only (the TAU group).

Hypotheses

1. In both groups we hypothesized weight gain, since both inpatient programmes focus on nutritional stabilisation.
2. In terms of cognitive and emotion task related performance after the treatment our hypothesis was that the CREST group would improve more than the TAU group.

Method

Ethical approval was obtained from the Oxfordshire REC NHS ethics committee (Ref: 08/H0606/58). Study participants were recruited from specialist inpatient eating disorder units receiving national referrals. Patients receiving CREST were recruited from the South London and Maudsley NHS Foundation Trust inpatient ward and patients receiving TAU were recruited from Manchester (Cheadle Royal Hospital).

Participants

Consecutively referred adult patients were offered participation in the trial if they had a DSM-IV (165) diagnosis. Patients were excluded from the study if they had an additional diagnosis of a learning disability, psychosis or major physical illness. Each participant was given a detailed information sheet about the study and signed consent forms were collected from each study participant.

Interventions

Participants in the London inpatient ward received CREST as detailed above, in addition to TAU. Participants in the TAU group received standard inpatient care with individual and group therapy. At both sites TAU involved typical inpatient care: nutrition management, dietetic input, occupational therapy, family work, individual cognitive behavioural therapy and group work on self-esteem and body image. In addition, TAU in London included individual work on psychological assessment and formulation. In Manchester, TAU additionally included: individual cognitive analytic therapy and schema therapy.

Assessments

Participants in both groups were assessed 10 days after admission to the inpatient wards (within the first 2 weeks, T_1). Participants were reassessed 10-11 weeks later i.e. at the end of treatment (T_2).

Demographic and clinical measures

Pre-morbid intelligence was assessed with the National Adult Reading Test (171). Clinical characteristics included BMI, illness duration, highest ever BMI and lowest BMI since onset.

Neurocognitive (Set-shifting, central coherence) and emotional processing tasks

Set shifting was assessed using the Brixton Test (148) and the Wisconsin Card Sorting Test (WCST) (172). Central coherence was assessed using the Fragmented Pictures Task (173) and the Group Embedded Figures Task (GEFT) (174). Emotion processing was assessed using the Reading the Mind in the Eyes Task (175) and the Pictorial Emotional Stroop Task (176).

Statistical analysis

All statistical analyses were performed in Stata 11. A linear mixed model was used to compare the two treatments. BMI and the six neuropsychological tasks were the outcome measures. Severity of illness (measured by BMI), duration of illness (years since diagnosis was established), IQ (measured by NART total score) and age were included as covariates.

Results

Patient Flow

In the CREST group, 46 participants completed the baseline assessments. Nearly one quarter of these (24%;N=11) dropped out of the treatment. Seventy-six percent (N=35) of the participants completed CREST, however 8.5% (N=3) did not participate in the post-treatment

assessment and 5.7% (N=2) were discharged before the post-treatment assessment was due. Thus, 65.2% (N=30) of CREST + TAU participants completed the follow up assessment . In the TAU group, 34 participants completed the baseline assessments and 73.5% (N=25) completed post-treatment assessments.

Patient Characteristics

In Table 15, patients' socio-demographic and clinical characteristics were compared using Wilcoxon Rank Sum tests. Both groups were similar in terms of age, IQ and severity of illness.

Table 15: Baseline demographic and clinical characteristics

	CREST (London)	TAU (Manchester)	
	m (*SD*)	*m* (*SD*)	*p*
Age (years)	26.1 (7.6)	26.0 (7.9)	0.85
IQ	105.8 (8.1)	104.5 (7.8)	0.31
Illness Duration (years)	10.6 (7.0)	9.9 (7.6)	0.52
Lowest ever BMI (kg/m^2)	12.0 (1.9)	12.9 (1.2)	0.13
Highest ever BMI (kg/m^2)	18.6 (3.5)	19.8 (3.2)	0.13

Within group changes

There were significant improvements in BMI in both TAU and CREST groups. In terms of neuropsychological task performance outcomes, there were significant improvements in both groups for the set shifting performance-based tasks (Brixton and WCST), significant improvements in the CREST group only for the Fragmented Picture Task (FPT), measuring 'bigger picture' information processing style. The TAU group showed poorer performance on the second 'bigger picture' related task (GEFT) and no significant differences were observed in either group on the remaining neuropsychological tests (Stroop andRME) measuring emotional processing. The detailed description of test results reported in Davies et al (177).

Between group changes

There were no significant differences between the groups concerning the change over time on any of the outcomes (details of the outcomes reported in (177))

Additional analysis

An additional analysis was conducted in CREST participants to identify if there was any difference in the baseline neuropsychological assessment scores between intervention completers, and those who dropped out. No significant differences were found between these two groups.

Discussion

This study aimed to assess the efficacy of the individual format of CREST for inpatients with AN. Both groups showed significant improvements in BMI as expected. Our hypothesis, that in within-group analyses neuropsychological measures would not change over time in the TAU group and would improve in the CREST group, was only partially supported by the results. Whilst the TAU group showed no change over time on central coherence (more 'bigger picture' thinking, less attention to detail) or emotion processing outcomes (less bias towards angry faces or recognition of emotions from the RME task), set shifting task performance did improve in this group (this supports the idea that cognitive flexibility improves with weight restoration). The CREST group also showed set-shifting improvements and additional improvements in global processing (this could be explained by the fact that CREST has introductory sessions on cognitive styles addressing global thinking style strategies). The results of the study showed that the TAU group became more detailed focused over time, while the CREST group remained stable in their information processing style (central coherence). There were no changes in emotion processing experimental outcomes in the CREST group (e.g. less bias towards angry faces and better recognition of emotions). In the between-group analyses there were no significant differences between the CREST and TAU groups on any of the neuropsychological domains or weight gain.

This study does not support previous findings suggesting that TAU does not improve set shifting (178), as the TAU group improved in set shifting in this study. This suggests that more longitudinal studies are required to assess the effects of TAU on set shifting across different inpatient groups.

It is possible that differences between the groups explain the improvements in cognitive flexibility following TAU and the non-significant differences between the groups on all measures. Although the groups in this study were comparable on sociodemographic and clinical characteristics, there was a trend in the CREST group towards a lower lowest lifetime

BMI and a lower highest ever BMI compared to the TAU group. Moreover, although the two groups were recruited from specialist inpatient services, the TAU group received intensive individual psychological input from a variety of treatment models as part of their TAU package (e.g. cognitive analytical therapy and schema therapy).

Limitations

This study was designed in a quasi-experimental format, which is less robust than a randomised control trial. A small sample size and several neuropsychological outcomes were clear limitations of the study.

Finally, there is evidence from the literature that self-reported measures correspond poorly with neuropsychological assessments (179). The benefits recognised by patients were not fully reflected in the neurocognitive assessments, which raises the issue of how to measure the outcomes of CREST. We could improve our assessment battery to include tests measuring emotion expression which is an area into which CREST taps and which has been found to be impaired in AN (163, 177, 180). Other important aspects of the CREST intervention are learning how to be with other people and communicating one's feelings. In future studies a measure of social anhedonia and functional outcomes will be more relevant in the context of measurable benefits of this intervention.

Conclusions

In summary, this study does not give clear evidence that the addition of CREST to a multi-faceted inpatient programme produces changes in neuropsychological task performance. Further studies are needed to corroborate these findings, using a larger sample size and a randomised controlled design with fewer, more targeted neuropsychological assessments. From the current study it seems that 'hot' cognition is harder to address and change in psychological treatment than is 'cold' cognition in the inpatient population with AN. A systematic review of the existing experimental measures for emotional tasks will inform future studies, enabling us to select fewer and more targeted outcome measures.

General discussion

CREST was designed to offer support to patients in ward settings who are physically and medically compromised and find it difficult to engage in psychological treatment. Our approach in designing this clinical intervention was based on both extensive input from

stakeholders: patients, clinicians and carers (181) and recent findings from experimental studies (16, 182, 183).

The three studies reported here used mixed methods to provide an initial evaluation of CREST in individual format. The overall results were mixed. The case study (Study 1) and qualitative work (Study 2) showed that inpatients valued and benefitted from the structured approach and taking simple steps to develop awareness and skills to manage emotions. In contrast, we found that the neuropsychological changes were not very impressive or easy to interpret (Study 3).

Following on from these findings, our future work will aim to revise the CREST manual in the light of service users' feedback and our clinical experience from delivering and supervision of the model. Revising the current version of the CREST manual will involve taking into account the qualitative feedback, specifically, removing the less relevant exercises (recognising other people's facial expressions in the social context as well as cold cognitive exercises) and expanding those that patients found to be most helpful (e.g. emotion vocabulary development, thinking, recognising and doing positive things). In addition, we will incorporate recent research findings, such as the lower emotional intelligence relative to the high IQ in groups of AN patients, poor facial expression of positive emotions, limited vocabulary for describing positive emotions, social anhedonia and extreme difficulties in private and social leisure activities (177, 184, 185). Finally, outcomes for the next stage (i.e. a randomised treatment trial) will be optimised. We will aim for a balance between experimental and self-report measures, and will use measures that are more tailored to the intervention content in order to detect changes after the treatment.

Chapter 6. A randomised controlled trial to evaluate the efficacy of adding a guided self-help intervention for carers of inpatients with anorexia nervosa

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Abstract

Word count: 173

Background: Families express a need for information and help to support people with severe and/or enduring anorexia nervosa (AN). We have developed a guided self-help, skills training intervention for carers (Experienced Carers Helping Others [ECHO]).

Objectives: To examine the impact of the addition of ECHO to standard inpatient care on carer and patient outcomes over time.

Method/design: Patients (over 12 years old) with a primary diagnosis of AN, and their carers, were ascertained from 15 inpatient services in the UK. Patients were randomised to either receive ECHO (a book, DVDs and 10 telephone coaching sessions per family) or treatment as usual. Patient ($n = 178$) and carer ($n = 268$) outcomes were measured at discharge and 6 and 12 months after discharge.

Results: Carers in the ECHO group spent less time care-giving, and had less burden and expressed emotion at discharge and/or 6 months. At 6 months, patients experienced a decrease in eating disorder (ED) symptoms and improved quality of life.

Discussion: Skills-based training improves both patient and carer outcomes.

Introduction

Anorexia nervosa (AN) develops in early adolescence and over 50% of cases have an illness that persists for over seven years (186). The group who have failed to respond to treatment, and/or those in whom there is high medical risk, receive inpatient care. The admission and discharge criteria and the form and content of inpatient care vary. For example, the practice in the UK has changed. In the UK, inpatient age at admission has increased since cohorts in 1959-64 (187-190), and inpatients present with more severe and long-lasting cases. The parameters of inpatient care are mainly driven by clinical consensus rather than evidence based decision making as there has been very little research into this. A recent exception is a randomised controlled trial (RCT) which compared standard inpatient care with a short period of inpatient care followed by day patient care for severely ill adolescent patients in the early stage of their illness. The study found similar one year weight outcomes between the forms of treatment but with less expense and better social adjustment with the inpatient/day patient intervention (191). This suggests that reducing the time separated from the family may be of benefit.

In the earlier stages of AN (less than three years duration), family based interventions offer the best patient results (192, 193). However, individuals who develop AN later in life or have an illness duration of more than three years do not respond as well to this intervention (192). Therefore there is uncertainty about whether and how carers should be involved in those having inpatient care at a later stage of the illness. Families request help and knowledge about the illness (194, 195) and experience high levels of burden and distress (196, 197). A variety of psychoeducational interventions have been developed to address this need and the data from a recent systematic review and meta-analysis of these interventions showed carers experienced less burden and distress following training. (198).

It is of interest to know whether these psycho educational interventions for carers have a secondary beneficial effect on the individuals with an eating disorder. Some of the interventions are based on a theoretical model suggesting that interpersonal factors, including carers' levels of expressed emotion (199) and accommodating and enabling behaviours (200), may contribute to the perpetuation of the illness (19, 20, 201). Experienced Carers Helping Others (ECHO) is a guided self-help, skills training intervention. A recent pre-test post-test study showed an improvement in carers' wellbeing after the intervention and, consistent with the theoretical framework (202), found that wellbeing increased as carers' expressed emotion,

accommodation and enabling decreased , (203). However, as yet there has been no controlled prospective study that has examined the validity of the extended model by examining whether the individuals with eating disorders (EDs) benefit from giving their carers guided self-help, skills training.

This study aimed to evaluate the impact of a psychoeducational intervention for the carers of patients in the severe and/or enduring stage of AN admitted to day or inpatient care for nutritional rehabilitation. Carers were randomised to receive ECHO plus treatment as usual (TAU) or TAU alone. Both carer and patient wellbeing and inpatient treatment was followed in the year following discharge. This RCT was registered with Current Controlled Trials ISRCTN06149665.

Hypotheses

The trial investigated the following experimental hypothesis regarding (P) and carer (C) outcomes.

Primary hypotheses

1. (*P*). Compared to TAU, patients with carers receiving ECHO will have be better at maintaining symptom improvement and will be less likely to relapse (measured monthly based on a body mass decrease of 2 points [BMI] or readmission to hospital from ED symptoms, whichever comes first).
2. (*C*). At 12-month follow up, carers with ECHO training will have less distress than carers with TAU.

Secondary hypotheses

1. (*P*). Compared to TAU, patients in the ECHO group will have a higher BMI and quality of life, as well as lower ED symptoms and distress.
2. (*C*). At all time points, carers in the ECHO group will report fewer negative parenting styles, less burden and time spent caregiving, and an increase in quality of life.

Method

Design

This is a pragmatic two-arm multi-centre parallel group RCT. A detailed account of the trial protocol, including the description of the ECHO carer intervention, has been published (202). Consenting carers from dyads meeting the inclusion criteria were randomly assigned to either ECHO (plus TAU) or TAU alone. Guidance for the ECHO intervention was delivered by "experienced" coaches (people with lived experience of eating disorders ($n = 15$) and post graduate psychologists (without clinical training [$n = 5$]) who were specifically trained and supervised. Recruitment involved 15 inpatient eating disorder units within the NHS. Baseline and discharge measures were collected, along with follow-up data at 6- and 12-months post-discharge. After ceasing intensive treatment, patients were considered 'discharged'. To meet this criteria, they had to receive inpatient, day-patient, or specialised residential treatment ≥ 4 days a week, and maintain this status for a minimum of 4 weeks. Those who transferred to general supported housing were included too. Data for whether patients completed treatment or discharged themselves were not accessible for all sites and are not reported.

Ethics and governance

Main ethics approval was granted by the Royal Free Hospital Ethics Committee (08/H0720/41) with site-specific ethics and governance approval for all participating sites. The study was adopted by the Mental Health Research Network (MHRN).

Randomisation

Carers of a patient were randomly allocated to one of the two trial arms (ECHO or TAU). The King's Clinical Trial Unit at King's College London conducted the randomisation and minimisation was used, stratified by study site (15 NHS England hospital units) and disease severity categories (one or both of BMI <15, presence of compensatory vomiting). Those in the TAU arm could access the intervention after finishing the study.

Recruitment

Patient outcome: One year relapse rates are around 70% in comparable patient populations (204), with rates dropping to 30-50% in some relapse prevention studies (205). A reduction in relapse rates of at least 20% following ECHO was considered clinically significant. To detect this decrease using a survival analysis log rank test at 2.5% significance (adjusting for patient relapse and carer distress) with 80% power, we would need 110 families per treatment arm to detect a hazard ratio of 0.58. The total sample size required from the power calculation was n

= 316 patients. The limited resources for this trial meant that the final sample size was $n = 178$ families. Thus the study is underpowered particularly for patient's relapse rates.

Carer outcome: In our pilot studies, the effect size of the decrease in distress for carers who received ECHO with telephone support was 0.55. We therefore predicted that the potency of the intervention should reach an effect size of 0.4 at a 12-month follow-up. For continuous outcomes, an effective sample size of 110 per arm would be able to detect an effect size of 0.42 or larger with 80% power using a t-test at the 2.5% (adjusting for two primary outcome tests) significance level.

Participating sites

This project involves 15 different centres. . Fourteen of the sites are eating disorder specialist inpatient wards in the UK (13 adult, one adolescent), and one is a general psychiatric ward with specialist ED staff (adolescent). One of the specialist sites makes local referrals to specialist ED inpatient wards in the UK. All were National Health Service (NHS) units, except one, which is a private collaboration accepting NHS referrals.

Participants

Patients admitted to the treatment facility with a primary diagnosis of AN or Eating Disorder Not Otherwise Specified with anorexic symptoms (EDNOS-AN) were approached. Agreement of at least one carer, (proposed by the patient) was required for participation in the study. (Carers are defined as someone who provides unpaid help and support to a child, partner, relative, friend, or neighbour, who could not manage without their help [www.carers.org]).

Inclusion criteria: DSM IV anorexia nervosa aged 12 years or above, able to speak and comprehend English. Exclusion criteria: no carer identified (at least one carer had to participate for the patient to be included, although all close carers were encouraged to take part), patient/ carers taking part in another treatment study, or discharged from their inpatient stay before baseline assessment completed. In addition, participants with a severe co-morbidity at time of admission (e.g. severe learning disability, medical problems diabetes psychosis) were not included in the study.

Recruitment

Patients were approached after admission by participating staff on the wards and offered study details. Informed consent was from both patient and carer. Clinical Support Officers

(CSOs) from the Mental Health Research Network (MHRN) supported recruitment of patients and administration of the project on eligible sites.

Interventions

ECHO

Participants in the ECHO arm received this intervention in addition TAU. The materials were sent and the coaching begun immediately after randomisation. ECHO uses a skills training approach consisting of a book (49) and five DVDs (three theoretical, two practical) that complement the skills offered in the book with role plays and practical examples (presented visually with audio voiceover). A detailed intervention description is described elsewhere (202, 206) and a professionally produced version is available through the charity SUCCEED (207).

The intervention package additionally included 5 telephone coaching sessions per individual (up to 10 per family e.g. mother and father). The coach contacted participants within two. Coaches were encouraged to complete the sessions within a five month period. Calls were made on a regular basis with time in between (e.g. two weeks) for carers to practice the skills. The time taken to complete calls varied between families depending on individual circumstances. The expectation was that telephone calls lasted up to 40 minutes with a minimum of five calls (per family) to have completed the intervention. Information on coaches, their training and measurement of quality assurance is described in the published protocol (202)

Treatment as usual (inpatient or day patient treatment)

The NICE guidelines specify several grade C recommendations about inpatient care (208) and NHS England has set minimal quality criteria for inpatient units For this study, day patients were defined as patients who required non-residential intensive specialist treatment (≥ 4 days a week).

Intervention Delivery

All correspondence with carers on the randomisation outcome was by post. Families in the ECHO group received an intervention pack with the book, five DVDS, and supporting documentation (a letter explaining their contact with the telephone coach, action/goal sheets, details on the transtheoretical model of change, frequently asked questions, and details for technical support). Those receiving TAU were informed they could access ECHO after

completing the study, and were given contact details for BEAT, the leading eating disorder charity in the UK.

Data collection

All participants (patients and carers) completed self-report assessments by post at inpatient admission, discharge, and at six, and 12-month time points post discharge. Finally, for the year following discharge, patients completed a short monthly assessment on core eating symptoms by telephone, email or post. Detailed information about data management is described in the published protocol (202).

Measures

Those completed by the patient are marked with a (*P*) and those completed by carers are marked with (*C*).

Primary outcomes

Relapse (*P*): Relapse is defined as a readmission to hospital for AN treatment or a drop of 2 points from discharge BMI measured on a monthly basis, whichever came first.

Depression, Anxiety and Stress Scale (DASS) (*P, C*): A 21-item self-report measure to assess mood state over the past 7 days using a 4-point Likert scale (95). Three subscales providescores for depression, anxiety and stress. Good reliability and validity is reported (209).

Secondary Outcomes

Short Eating Disorders Symptom Scale (SEED) (*P*): A short questionnaire measuring core eating disorder symptoms (e.g. weight, fear of fatness), relating to the degree of ED (AN or BN) symptoms. Good reliability and validity are reported (210).

Eating Disorder Examination – Questionnaire (EDE-Q) *(P): A* self-report measure assessing eating disorder symptoms over the previous 28 days (141). The scale yields both behavioural frequency data and information on specific eating disorder psychopathology. The EDE-Q has good reliability and validity in ED samples (211).

Motivation to change *(P):* Patients rate the importance of and confidence to change their eating disorder on a Likert scale (0-10).

World Health Organization – Quality of Life Questionnaire (short version) (*P, C*): The t WHOQOL-100 measures an individual's perception of their quality of life in 24 areas. Each facet is represented by one item, a 5-point Likert scale, pooled in four domains: Physical health, psychological, social relationships and environment. An additional two items evaluate the 'Overall Quality of Life and General Health'. The QoL questionnaire has good psychometric properties. (212).

Eating Disorder Symptom Impact Scale (EDSIS) (C): A 24 item self-report measure rates carers' perceptions of eating disorder specific burden using a 5-point Likert scale. A total burden score and subscales can also be calculated. The EDSIS has good reliability. (206).

Accommodation and Enabling Scale for Eating Disorders (AESED) (*C*): This 33-tem self-report measure measures the degree of accommodating and enabling behaviours to the eating disorder. A 5-point Likert scale is used. A total score and subscale scores can be calculated. This scale has good psychometric properties (200).

Family Questionnaire (FQ) (*C*): This 20-item self-report measures expressed emotion in carers with a 4-point Likert scale. Items relate to both criticism and emotional over-involvement. The FQ has good psychometric properties. (213).

Time spent caregiving (hours/month) (Care-ED) (*C*): This study utilized a semi-structured interview to report the time carers spend with specific demands of their caregiving role across five categories in an average month. Following thematic analysis of 22 female and male carers of someone with an ED describing the demands of their caregiving role, the following categories emerged: "medical", "food", "non-food/medical practical support", "emotional", and "communicating with non-ED professionals". Time spent caregiving is summed across domains to quantify the total amount of care provided to patients in hours/month.

Process evaluation outcomes

Acceptability of intervention (*C*): Carers provide quantitative (visual analogue scales) and qualitative feedback on their experience of the study, caring and, for those who received it, ECHO.

Patient feedback (*P*): All patients are asked to provide qualitative feedback on their participation in the study (e.g. methodology), their observations of their carers' responses to

the illness since their participation in the project, and their responses to their carers over the course of the study.

Reimbursement

Participants were reimbursed on completion of each set of questionnaires (Patients received £25, Carers received £10).

Statistical Analysis

The objective of the statistical analyses was the comparison of those offered ECHO with those allocated to TAU on a number of primary and secondary outcomes. The primary patient clinical outcome is "relapse". A linear change was assumed between monthly measurements of BMI and this was used to extrapolate the day of which two points were estimated to be lost. The variable is right censored since a relapse might not have occurred by the end of the study period (1 year) or follow-up data for BMI could be missing. If five consecutive BMI measurements were missed, time to relapse was censored.

The primary carer clinical outcome is distress (measured by the Depression, Anxiety and Stress Scale) at 12-months after discharge. To account for two primary outcomes group differences on these outcomes were tested at a significance level of 2.5%. Secondary patient and carer outcomes are continuous measures at discharge, 6-month or one year follow-up (see Measures: Secondary outcomes). All statistical analyses were based on the intention-to-treat principle, that is, participants were analysed in the treatment arm to which they were randomised irrespective of whether they received the allocated treatment Additionally, the statisticians were kept blind to treatment allocation as long as possible.

Time to relapse was analysed using Cox regression. Explanatory variables in this model were the variable of interest (treatment arm) and randomisation stratifiers (site and illness severity categories, based on binary BMI and vomiting). The effect of treatment is estimated by the hazard ratio of relapse comparing ECHO with TAU.

The continuous secondary patient outcomes were analysed using linear mixed models. The dependent variable is the outcome at the respective time point (e.g. BMI at 12 months post discharge) and (fixed) explanatory variables are given by treatment arm, baseline values of the variable under investigation (e.g. BMI at pre-randomisation) and randomisation stratifiers. The models can contain random intercepts for coaches (in ECHO) to allow for correlation in outcomes due to treatment being facilitated by the same coach. The models

were used to estimate differences between treatment arms at each time point. Standardised treatment effect estimates were calculated by dividing group differences by the common pre-randomisation standard deviation of the respective outcome.

Outcome variables contained considerable numbers of missing values; see Results section for details. We empirically identified a number of baseline variables that were predictive of missing values in outcome and also found that the primary carer not adhering to ECHO (coded "1" = completed at least five coaching sessions or read at least half the coaching manual, "0" = did not complete the intervention) was predictive of loss-to-follow up; see Results section for details. To allow for these processes driving missingness, in addition to allowing randomised group and values of the outcome under investigation at different time points being predictive of missingness multiple imputation (MI) using chained equations as implemented in the Stata command ice (214). This allowed us to include predictors of missingness (including the post-randomisation variable adherence) in the imputation step without having to condition on these variables in the analyses models (215).

The continuous carer outcomes were analysed in a similar fashion except that analyses needed to include up to two carers per family (a nominated first and second carer). To deal with this the analysis and imputation models described for patients were extended for carer outcomes: First, the analysis models contained additional random intercepts that varied at the level of the patient to allow for similar outcomes for carers of the same patient. Second, to ensure that correlations were also reflected in the imputed values imputations in ice were carried out at the level of the patient allowing for two outcome variables – one for the primary carer and another for secondary carer (set to missing when there was no second carer, with resulting imputed values discarded before analysis).

To evaluate the effect on primary carer outcome of receiving a sufficient level of (here an adherence score of "1") without bias the Complier-average causal ECHO effect (CACE) on carer distress was estimated using a two-stage least squares (instrumental variables) estimator (216).

<u>**Results**</u>

Participant Flow

This study represents a unique collaboration of major UK ED treatment centres and describes a large group (178 patients and 268 carers) severely ill patients with AN. The consort diagram for the study is shown in Figure 2.

Assessed for eligibility ($n = 599$)

Enrollment

PATIENT: Excluded ($n = 346$)
-Not meeting inclusion criteria ($n = 93$)
-Declined to participate ($n = 252$)
-Other reasons ($n = 1$)

Patient consent ($n = 266$)

Carers approached ($n = 476$)

CARER: Excluded ($n = 214$)
-Not meeting inclusion criteria ($n = 2$)
-Declined to participate ($n = 212$)

Carer consent ($n = 262$)

PATIENT: Excluded ($n = 69$)
-Carers declined to take part ($n = 69$)

Families randomized ($n = 178$)

Allocation

Allocated to TAU
Patients ($n = 92$)
Carers ($n = 134$)

Allocated to intervention
Patients ($n = 86$)
Carers ($n = 134$)

Discharge

Patient
Primary outcome (BMI) ($n = 80$) (87%)
Lost to follow-up ($n = 12$)
Carers
Primary outcome (DASS) ($n = 99$) (74%)
Lost to follow-up ($n = 35$)

Patient
Primary outcome (BMI) ($n = 82$) (95%)
Lost to follow up ($n = 4$)
Carers
Primary outcome (DASS) ($n = 93$) (69%)
Lost to follow-up ($n = 41$)

6 months follow-up

Patient
Primary outcome (BMI) ($n = 64$) (70%)
Lost to follow up ($n = 16$)
Carers
Primary outcome (DASS) ($n = 92$) (69%)
Lost to follow-up ($n = 7$)

Patient
Primary outcome (BMI) ($n = 65$) (76%)
Lost to follow up ($n = 17$)
Carers
Primary outcome (DASS) ($n = 92$) (69%)
Lost to follow-up ($n = 1$)

12 months follow-up

Patients
Primary outcome (BMI) ($n = 60$) (65%)
Lost to follow up ($n = 4$)
Carers
Primary outcome (DASS) ($n = 91$) (68%)
Lost to follow-up ($n = 1$)

Patient
Primary outcome (BMI) ($n = 52$) (60%)
Lost to follow up ($n = 13$)
Carers
Primary outcome (DASS) ($n = 91$) (68%)
Lost to follow up ($n = 1$)

Figure 2: CONSORT flow diagram (WP3)

Sample Characteristics

Patients

The majority of the patients were white (6% were Asian mixed). Twenty percent were married, 14% were in work and 41% had higher education. The majority (69%) were living with their carer and prior to admission 48% had > 21 hours of face-to-face contact per week with their carer. The patient group ($n = 178$) included cases from both adolescent ($n = 11$) and adult ($n = 167$) services. The median age of onset was 15 (range 5-45 years). The mean lowest ever BMI was 12.9 (1.8) kg/m^2. Median current age was 24.3 (range 12.5-62.7 years) with a median duration of illness of 72 months (range 9-480 months). The majority of cases ($n = 123$, 69%) had been ill for more than three years with a subset ($n = 83$, 55%) having a duration exceeding six years (enduring AN) (217). Co-morbidity with depression was 46% and 44% were on antidepressants. This was the first admission for approximately one third of the sample and 8% had five or more admissions.

The short term effects comparing admission and on discharge symptoms from inpatient care have been published (218). The median duration of the admission was 153.5 days (range 28-991 days) and one patient was not discharged t throughout the two years of the study.

Carers

A total of 268 carers ($n = 178$ primary carers, $n = 90$ secondary carers) were recruited ($n = 144$ mothers, $n = 81$ fathers, $n = 28$ partners, $n = 7$ siblings, $n = 5$ friends, $n = 3$ other relatives). The median age of the carers was 52.7 years (19.7-78.9) and 60% were female. Seventy-nine percent were married or living together, 63% were in work and 46% had higher education. Nineteen percent of the carers self-reported that they had suffered from an eating disorder themselves and 24% reported some sort of eating problems in the family other than that of the patient.

Randomisation

Patient and carer outcomes were well-balanced across groups. Roughly 25% at discharge, 30% at 6 months after discharge and slightly over one third of patients at 12 months showed missing questionnaire outcome data. At 12 months the proportion this ranged between 0.33 and 0.37 for the different scales. For the carers, the proportion of missing data was 2-4 percentage points greater at all outcome time points. The proportion of missing outcome data at 12 months ranged between 0.32 and 0.43. Logistic regression was used to explore the relationships between a dependent variable that represented whether outcome data were

present or missing at 12 months after discharge and a number of baseline demographic and clinical variables, such as participant gender and lowest ever BMI. Any variable that showed a statistically significant association with the dependent variable was included in the imputation step of the MI procedure. Non-adherence with ECHO was strongly associated with missingness, with odds ratios from 1.5 to 2.0 for patients' data and from 3.3 to 6.2 for carers' data.

A comparison of inpatient treatment post discharge of the patient groups (Carers with ECHO and Carers with TAU)

The ECHO group had shorter admission length (median = 148 days, range 28-991) compared to TAU group (median = 163 days, range 33-570) Mann-Whitney U test, z = -0.88, p = 0.38. The readmission rate was 26.7% (n = 23) in the ECHO group and 32% (n = 29) in the TAU group. Relapse in terms of readmission and/or fall in 2 BMI points occurred in 43% of the ECHO group and 52% of TAU. The median time to relapse for the ECHO group was 262 days and 240 days for TAU. Survival plots of the time to relapse showed two similar curves (see Figure 3). The TAU showed greater relapse-free survival initially. However, after approximately eight months the curves crossed over. Thus the study did not detect a statistically significant difference in survival curves and the main assumption of a Cox regression model, that the hazards are proportional, was broken (a Cox regression which relies on proportional hazards would give a hazard ratio of 0.82 in favour of ECHO and a p-value of 0.42 for the group difference).

Table 16 summarises the clinical outcomes and Table 17 provides estimated outcome differences between the two treatment arms for both patients and carers at all three time points.
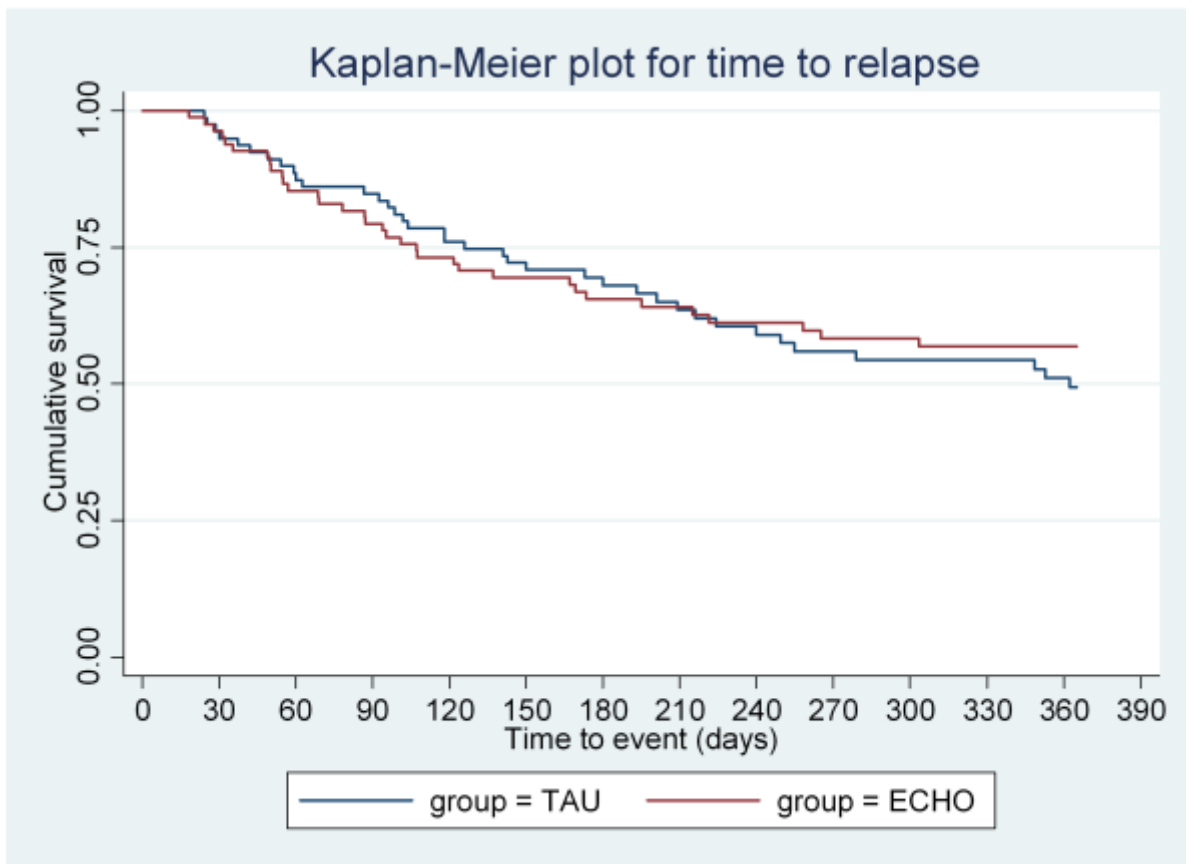
Figure 3: Kaplan-Meier curves for time to relapse

Table 16: Summaries of outcome measures by treatment arm and time point

	ECHO				TAU				Total			
	Baseline	Discharge	6 months*	12 months*	Baseline	Discharge	6 months*	12 months*	Baseline	Discharge	6 months*	12 months*
Patient data												
BMI (kg / m^2)	14.5	17.5	17..1•	17.3	14.3	17.4	17.1	17.0	14.4	17.5	17.1	17.2
(*P*)	(1.8)	(1.9)	(2.9)	(2.9)	(2.3)	(2.4)	(3.1)	(2.5)	(2.1)	(2.2)	(3.0)	(2.7)
WHO – Quality	10.7	11.7	11.9	11.8	10.5	11.6	11.1	11.4	10.6	11.7	11.5	11.6
of Life	(2.2)	(2.6)	(2.5)	(3.4)	(2.6)	(2.8)	(2.9)	(3.2)	(2.4)	(2.7)	(2.7)	(3.3)
Questionnaire												
(*P*)												
Eating Disorder	4.3	3.4	3.4	3.3	4.1	3.3	3.6	3.4	4.2	3.4	3.5	3.3
Examination (*P*)	(1.3)	(1.5)	(1.7)	(1.8)	(1.2)	(1.5)	(1.6)	(1.6)	(1.2)	(1.5)	(1.6)	(1.7)
Depression and	77.6	63.3	63.2	61.1	78.5	64.3	65.2	62.1	78.1	63.8	64.2	61.6
Anxiety Scale	(28.1)	(30.1)	(31.7)	(31.2)	(27.8)	(33.2)	(32.9)	(31.5)	(27.9)	(31.5)	(32.2)	(31.7)
(*P*)												
Carer data												
Depression and	29.6	30.5	26.4	26.2	31.5	34.5	33.2	30.9	30.5	32.5	29.8	28.5
Anxiety Scale	(25.6)	(25.1)	(22.9)	(23.6)	(26.7)	(28.3)	(25.5)	(29.7)	(26.1)	(14.3)	(24.5)	(26.8)
(*C*)												

Family Questionnaire (C)	48.5 (8.2)	46.0 (9.0)	44.4 (8.6)	43.8 (9.5)	47.9 (9.4)	48.0 (8.8)	46.8 (8.4)	45.0 (9.6)	48.2 (8.8)	47.1 (8.9)	45.6 (8.6)	44.4 (9.5)
Accommodating and Enabling Scale for ED (C)	47.7 (22.1)	40.7 (21.3)	35.5 (23.1)	33.1 (22.6)	47.3 (24.9)	43.9 (24.8)	41.5 (23.8)	37.7 (24.7)	47.5 (23.5)	42.4 (23.3)	38.5 (23.6)	35.3 (23.7)
Eating Disorder Symptom Impact Scale (C)	41.4 (12.5)	32.9 (14.6)	30.1 (15.1)	29.0 (16.5)	41.1 (14.2)	37.2 (13.8)	35.6 (14.2)	33.0 (16.5)	41.2 (13.4)	35.2 (14.3)	33.0 (14.8)	31.0 (16.6)
Time spent caregiving (hours / month) (C)†	70.5 (0-815.0)	25.2 (0.6-351.0)	22.0 (0-478.0)	17.5 (0-466.0)	70.6 (0-708.0)	25.0 (0.3-513.7)	31.9 (0, 378.0)	20.0 (0-379.0)	70.6 (0-815.0)	25.0 (0.3-513.7)	30.0 (0-478.0)	20.0 (0-466.0)
WHO – Quality of Life Questionnaire (C)	15.1 (2.3)	14.8 (2.3)	14.7 (3.1)	14.3 (4.0)	14.6 (2.4)	14.2 (2.4)	13.7 (2.7)	13.1 (3.8)	14.8 (2.3)	14.5 (2.4)	14.2 (2.9)	13.7 (3.9)

(*P*) patient reported; (*C*) carer reported. * time points refer to time since discharge, Mean (*SD*); †Median (range)

Table 17: Estimated treatment effects on patient and carer and outcome measures at all three post-randomisation time points

	Discharge				6 months after discharge				12 months after discharge			
	Est. group diff.‡	Test	95% CI‡	Stand. coef.‡	Est. group diff.‡	Test	95% CI‡	Stand. coef.‡	Est. group diff.‡	Test	95% CI‡	Stand. coef.‡
Patient data												
BMI (kg / m^2) (P)	-0.05	$z = -0.18$, $p = 0.86$	-0.57, 0.48	-0.02	-0.07	$z = -0.18$, $p = 0.86$	-0.82, 0.69	-0.03	-0.30	$z = -0.71$, $p = 0.48$	-1.11, 0.52	-0.14
WHO – Quality of Life Questionnaire (P)	0.13	$z = 0.35$, $p = 0.73$	-0.62, 0.89	0.05	0.91	$z = 2.05$, $p = 0.04$	0.04, 1.78	0.38	0.23	$z = 0.40$, $p = 0.69$	-0.90, 1.37	0.10
Eating Disorder Examination (P)	-0.12	$z = -0.59$, $p = 0.56$	-0.54, 0.29	-0.10	-0.47	$z = -2.09$, $p = 0.04$	-0.92, -0.03	-0.38	-0.40	$z = -1.46$, $p = 0.15$	-0.93, 0.14	-0.32
Depression and Anxiety Scale (P)	-2.74	$z = -0.68$, $p = 0.50$	-10.60, 5.13	-0.10	-4.45	$z = -1.03$, $p = 0.31$	-12.97, 4.06	-0.16	-1.58	$z = -0.32$, $p = 0.75$	-11.30, 8.13	-0.06
Carer data												
Depression and Anxiety Scale (C)	-0.54	$z = -0.18$, $p = 0.86$	-7.29, 6.21†	-0.02	-4.51	$z = -1.40$, $p = 0.16$	-11.74, 2.72†	-0.17	-3.24	$z = -0.97$, $p = 0.33$	-10.76, 4.28†	-0.12
Family Questionnaire (C)	-1.23	$z = -1.08$, $p = 0.28$	-3.45, 1.00	-0.14	-2.24	$z = -2.01$, $p = 0.05$	-4.43, -0.05	-0.25	-0.61	$z = -0.45$, $p = 0.66$	-3.31, 2.08	-0.07

Accommodating and Enabling Scale for ED (C)	-1.44	z = -0.51, p = 0.61	-7.00, 4.11	-0.06	-3.63	z = -1.00, p = 0.32	-10.77, 3.51	-0.15	-0.22	z = -0.06, p = 0.95	-7.59, 7.14	-0.01
Eating Disorder Symptom Impact Scale (C)^C	-3.98	z = -2.05, p = 0.04	-7.80, -0.16	-0.29	-3.42	z = -2.11, p = 0.11	-7.56, 0.73	-0.25	-2.16	z = -0.83, p = 0.41	-7.25, 2.93	-0.16
Time spent caregiving (hours / month) (C)	1.02**	z = 0.11, p = 0.91	**	0.01	0.63**	z = -1.98, p = 0.05	0.40, 1.00**	-0.34	1.04**	z = 0.15, p = 0.88	0.58, 1.90**	0.03
WHO – Quality of Life Questionnaire (C)	0.32	z = 1.20, p = 0.23	-0.20, 0.84	0.14	0.12	z = 0.41, p = 0.77	-0.69, 0.94	0.05	0.40	z = 0.62, p = 0.54	-0.88, 1.69	0.17

(*P*) patient reported; (*C*) carer reported. * time points refer to time since discharge ǂ coefficients represent estimated treatment effect of ECHO – TAU. †97.5% confidence interval (for joint primary outcome) ** Group effects represent factor change. Note: coach effects were found to be negligible and were therefore not included in the models.

A comparison of carers' wellbeing and burden in the ECHO and TAU condition

In all of the outcomes measured, the carers in the ECHO group had improved functioning. Carers in the ECHO group reported less distress than those in TAU but this was not statistically significant at any time point.

Time spent care giving was reduced 6-months post discharge and was significantly lower in the ECHO group (p = 0.05), effect size (ES) = -0.34. Expressed emotion was also significantly lower in the ECHO group at 6-months (p = 0.05), ES = -0.25. Burden was significantly lower in the ECHO group at discharge (p = 0.04), ES = -0.29.

At discharge, we estimated that carers' perception of ED burden in the ECHO group were 3.98 points (95% CI 0.16, 7.80 points) less compared to TAU. At 6 months after discharge, time spent caregiving in the ECHO group was 63% (95% CI 40, 100%) of that spent in the TAU group. At the same time point expressed emotion in the ECHO group was estimated as 2.24 points (95% CI 0.05, 4.43 points) less on the Family Questionnaire than in the TAU group.

A comparison of the clinical status post discharge of the patient groups (Carers with ECHO and Carers with TAU)

ED psychopathology and quality of life were significantly better in the ECHO group at 6 months ES = -0.38 and 0.38, respectively) but these differences were not significant at 12 months post discharge. At 6 months after discharge, we found ED psychopathology amongst the ECHO group to be 0.47 points (95% CI 0.03, 0.92 points) less than in the TAU group. At the same time point, we estimated quality of life as measured on the World Health Organisation questionnaire to be 0.91 points (95% CI 0.04,1.78) lower in the ECHO group compared to the TAU group. Estimated differences in distress and BMI pointed towards a beneficial effect of ECHO, but none of these effects could be shown to be statistically significant.

Important harms or unintended effects

Two patients (one from each trial arm) died during the course of the study.

Semi-structured open feedback

Patients

Six months post-intervention 102/178 (52 C; 50 TAU) semi-structured open feedback forms were returned from patients and analysed using Thematic Analysis (see Table 18). Overall >

75% of the sample reported positive benefits and changes in their interaction with carers and within this a greater proportion (66-75% were from the ECHO group). These aspects included more adaptive, open communication and understanding, continued support, motivation and encouragement, meal support, better goal setting and a calmer family atmosphere. Over a third reported empathy and concern, for their family (a greater proportion (65%) in the ECHO group).

Carers

At 6-months 148 (83%) (*n* = 73C; *n* = 75TAU) feedback forms were returned from carers and analysed using Thematic Analysis (see Table 19). Overall 27% of carers expressed appreciation for the research study 82.5% of these were in ECHO group. Interestingly, this aspect of the study revealed partial non-adherence to the trial protocol as seven carers in the treatment as usual group expressed appreciation for the skills training (suggesting that they had possibly purchased the book themselves but no coaching). Over half of the carers (64%) reported negative perceptions of services post-discharge support and the majority 60% were in the TAU group (TAU (*n* = 57; *n* = 38 C). In terms of reports on their observations on the individual with an eating disorder, improved communication was reported by 43% of carers (60% in the ECHO group) and acceptable functioning in 49% of carers (60% in the ECHO group). Overall, this suggests that information and skills-training improves expectations and perceptions of both services and the individual with an eating disorder.

Table 18: Qualitative feedback - patients

	Patients (*n*)		Utterances (Frequency)	
	CASIS	TAU	CASIS	TAU
Project involvement				
Positive aspects of participation	45	44	83	79
Problematic aspects of participation	31	34	48	48
Project interest and/or confusion	9	7	9	7
No impact (carer and/or self)	19	31	40	57
Suggestions for improvement	4	5	4	5
Perceived need/appreciation for carer support	16	11	25	13
Altruism	13	16	14	18
Perceived changes in carer style				
Reduced expressed emotion/anxiety	16	6	31	8
Greater understanding, awareness and coping abilities	31	22	75	33
Improved relationship and communication	23	13	43	27
More responsibility, space and trust	19	10	32	11
Perceived negative changes	4	12	4	18
Reductions in carer expectations/pressure	4	4	6	5
Reported general improvements	14	6	24	11
Helpful strategies				
Adaptive open communication and understanding	38	33	70	50
Continued support, motivation and encouragement	28	26	50	36
Concern for carer(s) and family	9	4	10	4
Increased responsibility, trust and space	17	15	24	35
Non-ED communication and behaviours	8	4	11	4
Calmer family atmosphere	8	7	9	8
Meal support	25	21	36	28
Positive role modeling	1	1	1	1
Practical help	13	17	16	23
Clear boundary setting and expectations	18	17	23	28
Reduced pressure and expectations	4	3	4	4
Collaborative problem solving and goal setting	7	5	10	5

Unhelpful strategies				
Food, weight and shape talk	11	11	14	13
High expressed emotion and anxiety	29	21	37	44
Detachment, avoidance and distance	15	11	28	18
Pressure of others' expectations	7	9	14	13
Intrusive, directive or controlling approach	11	7	14	8
Loss of the 'special' feeling	1	0	1	0
Lack of understanding, communication and confusion	4	9	4	14
Lack of clear boundaries	19	15	21	17
Problematic carer responses and behaviours (general)	13	8	22	12
Family involvement	0	2	0	2
Relationship with carers (general)				
Positive relationship, impact and coping abilities	36	3	92	97
Problematic aspects of relationship and support	22	31	67	76
Mixed reports	11	13	13	14
Dependent attachment	0	6	0	6
Loss of intimacy	1	1	1	1
Empathy and concern for carers' plight	20	11	37	17
Patient reflections				
Caring for an adult	5	7	5	10
Professional services	6	3	7	7
Recovery process	4	3	6	3
Own responsibility for recovery	3	5	4	8
Struggles and reflections on situation	7	9	9	11

Table 19: Qualitative feedback - carers

	Carers (*n*)		Utterances (Frequency)	
	CASIS	TAU	CASIS	TAU
Service provision and carer support				
Self-discharge	4	7	5	8
Negative perceptions of care, services post-discharge support	38	57	79	121
Acceptable aspects of post discharge support/services	33	27	50	44
Importance/appreciation of carer support and research	33	7	51	9
Unhelpful support/no need for support	5	4	6	4
Role perception and relationship with loved one				
Positive aspects of relationship	39	35	55	47
Negative or problematic aspects of relationship	12	25	14	40
Full-time caring and/or dependency	15	20	20	25
Continued emotional-practical support	54	55	93	117
Reduced caring role	37	31	52	50
Perceived carer impact	35	36	47	40
No change or little impact (self or impact on illness)	12	28	15	38
Familial role differentiation	7	11	11	14
Apathy and acceptance	1	9	1	10
Issues unique to partners	0	2	0	5
Perceived improvements in situation				
Reports of acceptable functioning in sufferer	44	29	76	47
Slower progress & determination	27	37	43	56
Improved communication and relationships	38	25	66	29
Reduced burden (practicalities)	3	3	3	3
Perceived carer changes				
Supporting independence and responsibility	22	24	30	36
Reduced high expressed emotion	25	20	38	25
Adaptive communication and techniques	13	11	16	11
Greater knowledge and understanding	17	15	18	15
Improved coping skills and self care	12	8	16	11

Boundary setting	5	4	6	4
Separating illness from person	4	3	4	3
Less ED talk	1	5	1	5
Continued difficulties and challenges				
Continued struggles and burden	46	48	86	135
Problematic behaviours, patient struggles or relapse	34	42	52	95
Impact on other family members and relationships	15	15	25	19
Concern for the future	6	15	7	22
Problematic carer responses	7	10	11	19
Readmission to hospital	7	11	7	15
Own health problems	6	10	11	17
Sense of loss	5	6	5	8
Poorer communication/relationships	3	6	4	7
Financial issues	5	6	6	6
Stigma	2	6	2	7
Carer coping practices				
Social support	41	40	58	60
Hobbies, work	18	16	19	19
Psychoeducation and self-care	20	15	29	21
Less contact, detachment or distraction	10	19	15	25
Spirituality	1	6	1	10

Discussion

The aim was to evaluate whether adding a guided self-help, skills training intervention (ECHO) for carers of people with severe and/or enduring AN is of benefit for both carer(s) and for the patient. Patients in the ECHO group had significantly reduced ED symptomatology and improved quality of life at 6 months with no BMI differences. Carers in the ECHO group had a greater reduction in their time care giving following admission and this was associated with a small/moderate reduction in carer burden and reduced expressed emotion. The majority of the sample (particularly from the ECHO group) reported positive benefits and changes in their interaction with carers and a third reported empathy and concern for their family.

We did not find statistically significant effects of ECHO in terms of our distal primary outcomes, patient relapse and carer distress, although differences were in the anticipated direction. It is possible that estimated differences were not found for our primary outcomes because we under-recruited. This will particularly impact binary/time to event outcomes such as our primary patient outcome relapse. In hindsight, due to extraneous variables associated with carer distress, perhaps a more ED specific outcome such as carer burden should have been used as the primary outcome for carers. It will be important to understand why ECHO effects on variables targeted by this carer intervention (e.g. on expressed emotion) were not translated into stronger effects on distal outcomes and as a next step we plan to carry out mediation modelling to investigate which hypothesised paths of our theoretical model were active.

In terms of services in the ECHO group there was less usage of services such as duration of admission, time and number of relapses/readmissions in the ECHO group and there was less dissatisfaction from carers about post-discharge care.

These findings suggest that a degree of sustained benefit can be obtained for patients with severe and/or enduring form of eating disorders following intensive treatment for nutritional rehabilitation. A previous qualitative study suggests that patients experience benefits from their parents participating in these interventions (219). The increase in BMI (2.1 kg/m^2 14% increase) at one year is smaller than that found in early intervention cases given inpatient/day patient care (3 kg/m^2) (191) but greater than that seen in outpatient studies with less medically compromised adults (1.4 kg/m^2) (217) (1 kg/m^2 4% increase) (156). (1.3 kg/m^2)

(127). On the other hand, the reduction (17%) in eating disorder psychopathology is less than that seen in outpatient care (38%, 135).

Approximately two thirds of the patients lived with their carers with approximately 50% having over 21 hours of contact time. The levels of parental distress, burden, accommodating enabling behaviour and expressed emotion at baseline were within the range of that reported in systematic reviews of carer functioning (196, 197).The changes in carer distress, burden and care giving behaviours are comparable to those found in the meta analysis from a recent systematic review of psycho educational interventions for carers (198). In the meta-analysis carer burden fell by 0.39 at the end of treatment and 0.56 at the end of follow up. On the other hand the change in distress DASS (ES = 0.12 at 6 months was less marked than found in previous studies (in the meta-analysis this was 0.31 at the end of treatment and 0.39 at follow up). Differences in the stage of illness of the patients and in the outcome measures used may explain this variation. It is noteworthy that there was a small increase in carer distress and fall in quality of life during the course of the study in the TAU group. The reduction in accommodating and enabling behaviour was similar to that found in the meta-analysis (0.2-0.5) of as was the fall in carers expressed emotion (0.3-0.4). In comparison with the high intensity of care that the patients were given the carers had a very low-intensity intervention. This could explain why the treatment effect occurs at 6 months and then attenuates at the end of 1 year follow-up.

Limitations

This sample is not necessarily representative of the target population as it only includes people who agree for their carers to be involved and who have carers who are willing to help. Moreover, the study includes patients at various stages of illness (19 % early and 55% enduring) and it is possible that these subsets have different responses to the interventions. For example, family therapy is only effective as an early intervention (192). Over half of the patients in this sample ($n = 83$, 55%) fulfil the criteria for being in a severe and/or enduring stage of illness. Such patients are considered to be resistant to all forms of treatment (220, 221). The sample was only powered to detect moderate overall differences in patient outcome. With 134 carers in each group and 0.025 alpha level (adjusting for multiple primary outcomes), we had 80% power to detect an effect size of 0.38.

Although there are standard quality criteria for inpatient care the treatment ethos does vary between services. For example, some services involve carers more than others. This may

have decreased the size of the effect. However, as the sample was stratified by site it would not have led to any bias in the interpretation of the results.

Strengths

This study used the strengths of a pragmatic randomised controlled design to examine the effects of adding a low intensity psychoeducational and skills training intervention for carers to inpatient care for AN. Furthermore, this is a multicentre study with the majority of NHS England specialised eating disorder centres participating. Considering that the number of patients with AN requiring inpatient care is small, the sample size of this study is unique.

Clinical implications

The possible added benefit for patients and for services attained from giving carers psychoeducational information has been rarely studied but this study suggests that this is an area that merits more attention. It is possible that increasing the intensity of the intervention and including it within the service model of inpatient care might produce improvements for services, patients and carers. This would mean that carers might become more involved in treatment for adults.

Conclusion

A low intensity psychoeducational intervention for the carers of patients at a severe and/or enduring stage of anorexia nervosa produced a decrease in burden and time spent care giving and a small decrease in distress. Unhelpful carer behaviours such as high expressed emotion were also decreased. Carers reported higher levels of functioning in the people with eating disorders. Moreover, patients had greater improvement in eating psychopathology and quality of life and noted positive changes in carer's behaviours. Patients felt more empathy for their carer. Moreover, carers dissatisfaction with services was lower in the ECHO group. It is possible that increasing the intensity of work with carers may have benefits for clinical services for patients in addition to benefits for carers themselves.

Chapter 7. An investigation of issues associated with physical activity in anorexia nervosa (WP4)

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Abstract

Objectives: This WP has examined physical activity (PA) in people with anorexia nervosa (AN) and associations between drive to exercise, eating disorder (ED) psychopathology, anxiety, endocrine measures and energy expenditure.

Method: Four groups of women participants were recruited: AN-outpatients ($n = 37$), AN-inpatients ($n = 18$), a group with anxiety symptoms ($n = 34$) and a healthy control group ($n = 30$). Actigraphy and self-report were used to measure PA, together with the drive and reasons for exercise, ED psychopathology, anxiety, stress, depression, body composition and BMI . Salivary cortisol was also measured and estimates were made of energy expenditure. Measures were made cross-sectionally and longitudinally over 24 weeks.

Results: ED and general psychopathology and biological parameters were consistent with group selection ie with diagnosis. The groups demonstrated a spread in PA, especially on data from self-report. Objective PA levels did not differ significantly between groups both crossectionally and longitudinally: nonetheless, AN groups reported higher total PA than HCs. The outpatients with AN reported more walking and moderate PA than HCs: inpatients with AN reported more walking but less moderate and vigorous PA than the other groups. In the two AN groups, drive to exercise was significantly higher: these groups also rated 'improving tone' as being important and enjoyment and health, as less important motivators to exercise. Estimates of energy expenditure due to exercise (EE) indicate that 400kcals/day would be at the upper end in patients with AN, out of a total energy expenditure of approximately 1600kcals/day

Discussion: Elevated PA has often been reported in AN but this may, in part be due to patients' peception of their activity rather than what is actually done. Drive to exercise in the AN groups seems to be more closely linked to ED psychopathology than to anxiety. Estimates of EE due to PA, provide guidance for therapists wishing to introduce exercise into therapy.

<u>Introduction</u>

Increased physical activity (PA) in AN can be loosely defined as deliberate exercise and/or indirect behaviours such as pacing and/or fidgeting. These behaviours however, do not have a well defined definition (222), yet may contribute to the maintenance of low BMI (223, 224) and non recovery at 2 years (225). High levels of PA prior to admission and following discharge and have also been reported to be associated with poorer outcome (226, 227). In relation to treatment outcomes, commitment to exercise is a problem in inpatients and engagement in excessive sport in outpatients may be a barrier to treatment (228). In addition, high PA may arise prior to illness (229, 230) and remain following recovery (223, 231). Therefore excessive exercise behaviours may also contribute to the aetiology of AN rather than simply being a symptom of the illness. Furthermore, as high PA levels are associated with lower BMIs in individuals recovered from AN (223), this may suggest the persistence of illness behaviours, or show that high levels of PA are a trait rather than a state marker.

Research findings on the prevalence of high levels of PA in AN is mixed. This may be due to different methodologies, perceptual differences in levels of PA undertaken in AN compared to controls or to high degrees of individual differences in exercise behaviours. Despite these differences, increased PA has often been reported in this patient group (230, 232-235). Recently, a study reported increased PA in a subgroup of AN patients only suggesting that high PA may not be a universal in this patient group (236).

The hypothesised drivers of increased PA in AN are cognitive desire to lose weight (223), to improve mood (228) and to reduce anxiety (237, 238). This is supported by the fact that women with AN are reported to value negative affect regulation as a motivator for exercise more than they value exercising to improve health and fitness (232, 239). Individuals with AN are also more likely to rate body tone, attractiveness and weight control as more relevant motivators than exercising for enjoyment (239). Thus, PA may be a deliberate and controlled behaviour that is intended to promote weight loss (240).

The idea that high PA is driven by anxiety in AN is supported by the often reported comorbidity of the two (241-243), and the fact that approximately 50% of AN patients also have a life-time history of anxiety disorder (244, 245). In some AN patients, anxiety disorders are reported to predate the onset of the ED (243, 246), are associated with lower BMI (247) and poorer outcome (248). Therefore, anxiety may be a vulnerability factor that is independent of nutritional state (243). In terms of PA, an association between anxiety and

high levels of PA has been reported in AN patients. Further support for the idea that anxiety may be a driver for PA in AN comes from reports that PA helps to reduce depression, stress and anxiety in adolescents (249) and adults (238).

This study examined levels of PA, drive to engage in PA, motives for exercise, and a number of associated physiological and psychological measures in female patients with AN in healthy controls (HC) and in a group with moderate levels of anxiety). The study had the following hypotheses:

1. Subjective and objective measures of PA levels together with the drive to exercise will be increased in AN patients compared to HC and to the anxious group: these findings will be present both crossectionally and longitudinally over 24 weeks
2. Eating disorder (ED) psychopathology and anxiety will be associated with PA levels
3. Reasons for exercising will differ between groups.
4. In patients with AN, estimates of energy expenditure due to PA will show that less than 500kcals/day are used

Methods

Participants

Women were recruited as four groups: inpatients ($n = 18$) and outpatients ($n = 37$) with a diagnosis of AN, individuals experiencing moderate anxiety ($n = 34$) and healthy controls ($n = 30$). AN patients (binge-purging or restricting sub-type) with BMIs of <17.5 kg/m^2 were recruited from in and around London (from specialist ED services). These services included outpatient treatment ($n = 26$), daycare ($n = 10$) and inpatient treatment ($n = 18$). Patients attending daycare treatment were grouped with the outpatient participants. Anxiety and control participants were recruited via an email circular to students and staff at King's College London. Anxiety participants were screened using the General Anxiety Disorder GAD-7 questionnaire, and those with a score of 10 or more were recruited into the study. Participants had a mean age of 27 in the anxiety group (range 18-54), 29 in the combined AN groups (range 18-67) and 29 in the HC (range 20 – 52). All were English speaking. Recruitment commenced following approval by the local ethics committee (09/H0807/4). All participants provided informed consent

Measures

All participants provided data on the following measures:

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Demographic information

Contact details, ethnicity occupation, marital status, physical or mental health problems, lifestyle habits such as drinking and smoking.

Weight and height

Height and weight were measured and used to obtain BMI (weight [kg]/height [m]^2).

Structured Clinical Interview for DSM (SCID-I/P)

This is used to diagnose DSM-IV axis I disorders (250). Section H of the research version (SCID-I/P, Patient Edition) was used to establish a diagnosis of AN.

Eating Disorder Examination-Questionnaire (EDE-Q)

This questionnaire (self-report) has been validated in ED studies (141). It provides a global score and four subscale scores (weight and shape concern restraint, eating),).

Depression Anxiety Stress Scale 21-version (DASS)

This measure (a self-report questionnaire) assesses depression, anxiety and stress (251, 252). Scores determine level of severity for each sub-scale: normal, mild, moderate, severe and extremely severe.

International Physical Activity Questionnaire (IPAQ)

This questionnaire uses self report. It asks participants to estimate days and minutes spent sitting, walking, moderately and vigorously exercising per week. Number of days is multiplied by number of minutes on average spent engaging in each level of exercise to give an estimate (mins/week) at each level. These are summed to give a total amount of PA (mins/week). Where participants responded - 'I don't know/unsure', total scores were not calculated. A short version of this measure was used, and has been reported to have good international reliability and validity (253). This questionnaire has been used to estimate PA in other studies of ED (254, 255).

Commitment to Exercise Scale (CES)

This 8-item Likert-scale based questionnaire assesses commitment to exercise. It measures the degree to which a) feelings of well-being are influenced by exercising, b) adherence to exercise is maintained even in the face of adverse conditions, and c) exercise regimens interfere with social life (256). It has been used in ED (233, 257, 258).

Obligatory Exercise Questionnaire (OEQ)

This was used to determine the frequency with which participants experience obligatory and compulsory thoughts, feelings and exercise behaviours (259). The measure has 20 items where 1 = never, 2 = sometimes, 3 = usually, 4 = always, giving a possible maximum score of 80. Higher scores indicate higher obligation and drive to exercise. The measure has good validity and reliability (260) and has been used in ED and general population samples (261-263).

Exercise Addiction Inventory (EAI)

This measure (self report) assesses exercise attitudes and its impact on one's life (264). It has 6 items where 1 = strongly disagree and 5 = strongly agree, giving a possible maximum score of 30. A higher score indicates greater likelihood of "exercise addiction". The EAI is a reliable and valid tool for assessing risk of exercise addiction (264, 265).

Reasons for Exercise Inventory (REI)

This assesses the importance of 7 reasons to exercise: improving physical attractiveness improving body tone, improving mood, enjoyment, weight control, health and fitness. Each subscale has three or four items: 1 = not at all important and 7 = extremely important, and an average for each sub-scale is obtained (266). It has been used in studies of AN (232).

Body composition

An Inbody 3.0 Biospace Co. LTD machine was used to measure, skeletal muscle, body fat, total body water and bone mineral content in all participants. It is a portable device, non-invasive and uses electrical impedance to obtain the measures.

Actimetry

An actometer device (Actiwatch AW4, Cambridge Neurotechnology, Cambridge, UK) was worn continuously by each participant. It was worn on the non - dominant wrist, to measure PA over 7 days. This method has been used by other groups assessing PA in ED (267, 268). Average and peak activity scores were obtained by Actiwatch Sleep Analysis (2001) software.

Cortisol

Salivary cortisol was measured by obtaining weekly salivary samples in salivettes. Participants were asked to chew for one minute on a small cotton swab. As cortisol peaks in the morning, this was done ten minutes after waking and before smoking or eating breakfast..

Leptin

Serum leptin levels were measured in AN and HC participants only. Blood samples were collected weekly and were sent to the Dept of Clinical Biochemistry in King's Pathology Lab for analysis.

Data analysis

Five participants from the HCs with a BMI < 18.5 kg/m^2 and and six from the anxiety group with EDE-Q global scores >2.8 (269) were not used in the analyses. Group means were compared using one-way ANOVAs and Tukey post-hoc tests. Kruskal-Wallis tests and post-hoc Mann-Whitney tests using Bonferroni corrections were used to compare means for variables that violated parametric assumptions (EDE-Q, DASS, IPAQ and body fat). Pearson's rank correlations were used to infer relationships between variables before hierarchical multiple regressions were performed, with drive to exercise as the dependent variable.

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Results

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Group differences in outcome measures

EDE-Q and DASS

AN outpatients (AN-OP) and inpatients (AN-IP) had higher scores than the anxiety group and the HC on EDE-Q total score ($p < 0.001$) and across the 4 sub-scales ($p < 0.001$) (see Table 20). Restraint and eating concern scores were lower in the AN-IP group, yet differences between AN groups were not significant. The group with anxiety had higher scores than the HC on all EDE-Q subscales, and these were significantly higher for eating concern ($n = 55$, $F(3) = 2.76$, $p < 0.01$).

HCs were in the expected range for the DASS sub-scales (0-7). but the group with anxiety scored in the moderate- severe range for anxiety (7-12) and in the moderate range for stress and depression (6-9). The AN- outpatients scored 'severe' on all 3 sub-scales (8-16) and inpatient group had scores that assessed them as "severe-extremely severe" for depression (11-14+) and "extremely severe" for stress and anxiety (>10 and >17 respectively).

There were significant between group differences in total DASS scores ($F(3) = 56.14$, $p < 0.001$), and for the depression ($F(3) = 55.83$, $p < 0.001$), stress ($F(3) = 45.1$, $p < 0.001$) and anxiety ($F(3) = 49.44$, $p < 0.001$) subscales (Table 20). The AN groups reported higher anxiety, depression, and stress levels than the HC ($p < 0.001$). AN- outpatients (but not

inpatients) had higher depression scores than the anxiety group ($F_{(3)} = 3.2$, $p < 0.01$). The anxious and the AN groups did not significantly differ on other DASS scores. The anxiety group were higher than HCs on total DASS score ($F_{(3)} = 5.71$, $p < 0.001$) anxiety ($F_{(3)} = 5.55$, $p < 0.001$), depression ($F_{(3)} = 5.45$, $p < 0.001$), and stress ($F_{(3)} = 5.09$, $p < 0.001$).

Table 20: Diagnostic and psychological measures

	HC ($n = 27$)	Anxiety ($n = 28$)	AN-OP ($n = 35$)	AN-IP ($n = 17$)
EDE-Q (Total)	0.7 (0.7)	1.2 (0.9)	4.2 (1.2)	4.01 (1.2)
DASS (Total)	6.2(6.3)	27.1 (11.6)	34.9(12.7)	39.1 (18.4)

Values are means and standard deviations (*SD*)

This table is adapted from: Keyes, A., Woerwag-Mehta, S., Bartholdy, S., Koskina, A., Middleton, B., Connan, F., . . . Campbell, I. C. (2015). Physical activity and the drive to exercise in anorexia nervosa. International Journal of Eating Disorders, 48(1), 46-54.

Physiology

In the AN-OPs, BMI was consistent with diagnosis ($M = 16.04$, $SD = 1.44$). 97% were below normal ranges of body fat mass and 67% were below normal muscle mass ranges i.e. muscle was relatively conserved. 25% of AN-OPs had below normal ranges of bone mineral content (BMC). All AN-IPs were below normal fat mass ranges, 81% were below normal muscle ranges and 56.3% were below normal BMC ranges (presumably reflecting illness severity).

HCs were lean and fit as a group: 44% were below normal fat mass ranges (kg) and 26% were above normal muscle mass ranges (kg) for age and gender. The anxiety group were similar: 43% were below the normal fat mass range and 21% were above the normal muscle mass range for age and gender. However, anxiety participants had a larger range in BMI (a *SD* of 3.88 vs 1.5). No anxiety participants had BMC lower than the normal range.

The groups differed significantly in terms of BMI ($F_{(3)} = 63.32$, $p < 0.001$), muscle ($F_{(3)} = 27.6$, $p < 0.001$), body fat ($F_{(3)} = 69.8$, $p < 0.001$) total body water ($F_{(3)} = 26.81$, $p < 0.001$) and bone mineral content (BMC) ($F_{(3)} = 37.08$, $p < 0.001$) (see Table 21). On all body composition measues, AN participants differed from the HC and anxiety groups ($p < 0.001$). BMI did not differ significantly between the two AN groups, but the AN-OPs had

significantly lower BMC ($p < 0.01$). The anxiety group and the HCs were similar in terms of body composition.

Table 21: Physiology

	HC (*n* = 27)	Anxiety (*n* = 28)	AN-OP (*n* = 35)	AN-IP (*n* = 17)
BMI	21.2 (1.5)	22.24 (3.9)	16.0 (1.4)	14.1 (2.1)
Body fat (kg)	12.4 (5.0)	13.4 (7.7)	4.1 (2.8)	1.9 (1.6)
Skeletal muscle (kg)	28.5 (5.5)*	26.4 (2.9)	21.5 (3.5)*	19.1 (3.1)*
Bone mineral content	3.1 (0.4)	3.2 (0.4)	2.5 (0.4)	2.1 (0.4)
Total body water (litres)	34.3 (3.9)	34.5(3.2)	28.7 (4.2)	26.6 (3.5)
Resting metabolic rate	1431.1 (125.9)	1398.6 (96.6)	1221.8 (125. 4)	1151.0 (108.2)

*HC (*n* = 26), AN-OP (*n* = 34), AN-IP (*n* = 16), BMI = Body Mass Index Values are means and standard deviations.

This table is adapted from: Keyes, A., Woerwag-Mehta, S., Bartholdy, S., Koskina, A., Middleton, B., Connan, F., . . . Campbell, I. C. (2015). Physical activity and the drive to exercise in anorexia nervosa. International Journal of Eating Disorders, 48(1), 46-54.

Physical Activity (PA)

Actimetry: an objective measures of PA

The actimetry showed all groups had similar levels of activity (average and peak activity) (see Table 22) and there were no significant between group differences (average PA: $F(3) = 0.46$, > 0.05; peak PA: $F(3) = 0.26$, $p > 0.05$). The outpatient group had higher peak and average activity levels than the inpatient group (average: AN-IP, $M = 223.63$, $SD = 61.67$, $n = 10$; AN-OP, $M = 249.73$, $SD = 73.96$, $n = 27$; peak: AN-IP, $M = 3607.1$, $SD = 507.83$, $n = 10$; AN-OP, $M = 3961.15$, $SD = 1329.39$, $n = 27$), but these differences were not significant (both $p > 0.013$).

Table 22: Actigraphy data

		HC		Anxiety		AN- OP		AN- IP
	n	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*
Average PA	23	250.2 (61.5)	23	249.4 (63.1)	27	249.7 (74.1)	10	223.6 (61.7)
Peak PA	22	3971.3 (1350)	22	3657.1 (1727.0)	27	3961.2 (1329.4)	10	3607.1 (1507.8)

PA values are counts /minute

This table is adapted from: Keyes, A., Woerwag-Mehta, S., Bartholdy, S., Koskina, A., Middleton, B., Connan, F., . . . Campbell, I. C. (2015). Physical activity and the drive to exercise in anorexia nervosa. International Journal of Eating Disorders, 48(1), 46-54.

Table 23: IPAQ scores [mins])

	HC		Anxiety		AN-OP		AN-IP	
	Mean (SD)	*N*	*Mean (SD)*	*n*	*ean(SD)*	*n*	*Mean (SD)*	*n*
7 days:								
PA (Total)	489.7 (378.7)	26	699.5 (654.1)	26	942.2 (598.6)	22	768.9 (887.3)	14
Walking	290.7 (336.1)	26	497.9 (607.5)	26	571.4 (393.4)	27	629.7 (712.4)	15
Moderate	70.0 (85.0)	26	125.7(143.6)	28	219.9 (308.1)	25	67.3 (216.8)	15
Vigorous	124.8 (141.4)	26	82.6 (125.5)	28	163 .0(334.0)	31	58.0 (216.5)	15
Over 5 days:								
Sitting	1872.2 (649.0)	27	2088.0 (748.7)	25	1597.8 (955.8)	23	1406.3 (625.9)	8

This table is adapted from: Keyes, A., Woerwag-Mehta, S., Bartholdy, S., Koskina, A., Middleton, B., Connan, F., . . . Campbell, I. C. (2015). Physical activity and the drive to exercise in anorexia nervosa. International Journal of Eating Disorders, 48(1), 46-54.

IPAQ scores – self reported physical activity

Both of the AN groups recorded higher levels of total PA (min/week), than HCs (by 57-92%) (Table 23), and the difference between the outpatient group and HC ($F(3) = 3.05$, $p < 0.01$) was significant. Both outpatient and inpatient AN groups reported doing more walking than HCs (250% and 95% higher respectively), but the difference was only significant between OPs and HCs ($F(3) = 3.18$, $p < 0.01$). The outpatient group also reported engaging in more "moderate" exercise than HCs (>3-fold higher) but the difference was not significant. The inpatient group recorded engaging in less "moderate" exercise than the anxious group ($F(3) = -2.99$, $p < 0.01$) and less "vigorous" activity than HC ($F(3) = -2.89$, $p < 0.01$) and the anxiety group ($F(3) = -2.74$, $p < 0.01$). The inpatient group reported that they engaged in less moderate and also less vigorous activity than the outpatient group. Finally, the anxiety group, recorded higher amounts of total activity (by 43%), moderate activity (by 80%), walking (by 71%), and less vigorous activity (by 34%) than HCs, but none of these differences were significant.

Comparison of subjective and objective measures of PA

There were no large between group differences in objective measures of PA (total or peak activity), but subjectively (as assessed by the IPAQ), the AN and anxiety groups reported undertaking more activity. In addition, in each group, the range is wider at every level of self-reported activity compared to the actimetry measures. Standard deviations (*SD*) in subjective total PA are 77% (HC), 94% (anxiety group), 64% (AN-OP) and 115% (AN-IP), while comparable *SD*s from objective measures of average PA (actimetry) are 24%, 23%, 29% and 27% respectively.

Drive to exercise

Both the inpatient and outpatient groups had higher scores than the anxious group and the HC on the CES ($F(3) = 9.54$, $p < 0.001$), the EAI ($F(3) = 8.67$, $p < 0.001$) and the OEQ ($F(3) = 6.86$, $p < 0.001$) (Table 24). These questionnaires have slightly different elements but all three show high correlations ($r = 0.87$, $p < 0.01$), hence, we have created a 'global drive to exercise' (GDES) as single score. It was calculated in the following way. Average scores for each questionaire were converted to a % of the highest score by any participant, and averages of these three percentages were then obtained: this has been used previously to create amerger related scales e.g. for anxiety and depression (270).

Significant between-group differences are observed in drive to exercise ($F(3) = 9.42$, $p < 0.001$). Both the outpatients and the inpatients had significantly higher scores than the HC and the group with anxiety ($p < 0.001$). No significant differences were seen between anxious participants and HC or between inpatient and outpatient groups in their drive to exercise.

Table 24: Scales measuring drive to exercise

	HC ($n = 27$)	Anxiety ($n = 28$)	AN-OP ($n = 35$)	AN-IP ($n = 17$)	AN Groups ($n = 52$)
GDTE (%)	40.9 (12.3)	45.7 (11.3)	61.7 (23.0)	65.9 (30.0)	63.1 (25.3)
CES	0.3 (0.2)	0.3 (0.2)	0.5 (0.2)	0.6 (0.3)	0.5 (0.3)
OEQ	37.5 5.9)	41.1 (7.2)	48.1 (14.0)	51.3 (18.3)	49.1 (15.4)
EAI	11.2 (4.4)	13.1 (3.9)	18.3 (7.4)	18.5 (9.7)	18.4 (8.1)

EAI = Exercise Addiction Inventory [max. score = 30], CES = Commitment to Exercise Scale [max. score = 1], GDTE = Global Drive to Exercise, OEQ = Obligatory Exercise Questionnaire [max. score = 80], Values are expressed as means and SD (in brackets)

This table is adapted from: Keyes, A., Woerwag-Mehta, S., Bartholdy, S., Koskina, A., Middleton, B., Connan, F., . . . Campbell, I. C. (2015). Physical activity and the drive to exercise in anorexia nervosa. International Journal of Eating Disorders, 48(1), 46-54.

Reasons for exercise

There were between group differences for enjoyment ($F(3) = 2.91$, $p < 0.05$) and for health ($F(3) = 5.42$, $p < 0.01$) (Table 25). Between group differences for exercising for attractiveness approached significance ($F(3) = 2.64$, $p = 0.054$). Exercising for health reasons was less important for the outpatient group than for HC and the anxiety group (HC vs AN-OP, 4.83 vs 3.55, $p < 0.013$; anxiety vs AN-OP 4.79 vs 3.55, $p < 0.013$). Using exercise for enjoyment and to improve attractiveness was rated less important in the outpatient group than in the group with anxiety (attractiveness: $M = 3.11$ vs 4.39; enjoyment: $M = 2.20$ vs 3.17). Results were not however significant after applying Bonferroni corrections ($p = 0.47$ and 0.41). Finally, exercising to improve tone was more important in the two patient groups and the anxiety group than in the HCs (e.g. HC vs AN-OP, $M = 3.44$ vs 4.70), but these differences were not significant ($p = 0.056$).

Table 25: Reasons for exercise inventory

scales	HC (n = 27)	Anxiety (n = 34)	AN-OP (n = 32)	AN-IP (n = 15)	AN Groups (n = 47)
Weight control	4.2* (0.9)	4.7 (1.1)	4.6* (2.2)	5.0 (1.7)	4.7* (2.1)
Fitness	4.5 (1.2)	4.4 (1.5)	4.02 (1.8)	4.2* (2.0)	4.1* (1.8)
Mood	4.7 (1.5)	4.6 (1.8)	4.7 (1.7)	4.9* (2.1)	4.8* (1.8)
Health	4.8 (1.3)	4.8 (1.4)	3.6 (1.7)	3.7 (1.7)	3.6 (1.7)
Attractiveness	3.3 (1.9)	4.4 (1.8)	3.1* (1.8)	3.4* (2.3)	3.2* (1.9)
Enjoyment	2.8 (1.5)	3.2 (1.6)	2.2 (1.2)	2.2 (1.2)	2.2 (1.2)
Tone	3.4 (1.5)	4.2 (1.7)	4.7 (1.9)	4.2 (2.5)	4.5 (2.1)

, *HC $n = 30$, AN-OP: weight control $n = 26$, attractiveness $n = 31$, AN-IP $n = 14$, AN Groups: weight control $n = 51$, fitness & mood $n = 46$, attractiveness $n = 45$ Values are means and SD

Endocrine data

A significant between group difference in cortisol was observed ($F(3) = 2.73$, $p < 0.05$) (Table 26). The inpatient group have significantly higher cortisol than HCs ($p < 0.05$). No significant difference in cortisol was observed among the other groups ($p > 0.05$). Cortisol concentration and the DASS anxiety score were weakly correlated at baseline, and this approached significance ($n = 100$, $r = 0.19$, $p = 0.07$) across the group as a whole. When groups were analysed separately, no significant correlations were found between and the DASS anxiety score and baseline cortisol (HC: $n = 30$, $r = -0.05$, $p = 0.81$; ANX: $n = 33$, $r = 0.21$, $p = 0.25$; AN-OP: $n = 26$, $r = 0.1$, $p = 0.65$; AN-IP: $n = 11$, $r = -0.19$, $p = 0.58$).

Table 26: Cortisol and leptin data

	HC		ANX		AN-OP		AN-IP	
	Mean (SD)	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*	*Mean (SD)*	*n*
Cortisol (nmol/L)	10.0 (3.7)	30	11.4 (10.4)	31	12.3 (5.6)	26	17.9 (11.7)	11
Leptin (ug/L)	8.9 (4.7)	14	Not measured		2.8 (2.4)	30	2.6 (3.5)	16

Serum levels of leptin were measured in the two AN groups and HCs only. There was a significant between group difference in leptin ($F(2) = 18.55$, $p < 0.001$), in that both the

inpatient and outpatient groups had significantly lower leptin concentrations than HCs ($p < 0.001$): AN-OP and AN-IP groups did not significantly differ in concentrations of leptin. Across the whole sample, there was a significant correlation between leptin and body fat (%) ($n = 57$, $r = 0.72$, $p < 0.001$). Within group analysis revealed significant correlations between leptin and percentage body fat in each group: HC $n = 14$, $r = 0.71$, $p < 0.01$; AN-OPs $n = 29$, $r = 0.57$, $p < 0.001$ and AN-IPs $n = 14$, $r = 0.55$, $p < 0.05$.

Associations between outcomes

Subjective and objective measures of activity

When all participants were considered together, average activity (actimetry) was not correlated with total reported activity (IPAQ) and secondly, peak activity (actimetry) was not correlated with levels of reported vigorous activity. There was a significant but weak correlation between average activity (actimetry) and reported time spent walking ($n = 72$, $r = 0.24$, $p < 0.05$).

Within group analysis showed that for the HC, the anxiety group and the AN-OPs, there were no significant correlations between average/peak activity (actimetry) and any levels of self-reported activity. In the AN-IP group, however, there was a strong correlation between the average activity (actimetry) and self-reported total activity ($n = 9$, $r = 0.76$, $p < 0.02$) and walking ($n = 9$, $r = 0.74$, $p < 0.02$).

Relationship between actimetry data and other measuress

Across the study sample as a whole, there were no significant correlations between actimetry scores and other measures (e.g. DASS, EDE-Q, drive to exercise and REI). Within group analysis showed that when the two patient groups were combined peak activity correlated with EDE-Q global scores ($n = 36$, $r = 0.37$, $p < 0.05$). No significant associations were seen between actimetry data and other variables in all other groups.

Self-reported activity (IPAQ) and other measuress

Self-reported total activity, when examined across the whole group was weakly correlated with global EDE-Q score ($n = 86$, $r = 0.27$, $p < 0.01$) and with exercising to improve tone ($n = 83$, $r = 0.25$, $p < 0.02$). No significant associations were found between any levels of self-reported activity and other variables when within groups analysis was performed.

Drive to exercise and other variables

Drive to exercise may be an important pathological variable and as we used three scales to create a single measure (GDES), it was used as one of our main variables.

Across the whole group, drive to exercise (GDES) was most highly correlated with self-reported total activity ($n = 86$, $r = 0.39$, $p < 0.01$). In addition, correlations were present between drive to exercise and self-reported walking ($n = 94$, $r = 0.25$, $p < 0.02$), moderate activity ($n = 94$, $r = 0.29$, $p < 0.01$) and vigorous activity ($n = 102$, $r = 0.37$, $p < 0.01$). All these correlations were, however, less than 0.4.

In the AN groups combined, drive to exercise correlated with self-reported total activity ($n = 35$, $r = 0.52$, $p < 0.01$), self-reported walking ($n = 42$, $r = 0.37$, $p < 0.02$) and the following REI sub-scales: weight control ($n = 50$, $r = 0.55$, $p < 0.01$), fitness ($n = 46$, $r = 0.54$, $p < 0.01$), mood ($n = 46$, $r = 0.74$, $p < 0.01$), health ($n = 47$, $r = 0.43$, $p < 0.01$) and to improve tone ($n = 47$, $r = 0.44$, $p < 0.01$). In addition, correlations were seen between drive to exercise and vigorous activity ($n = 47$, $r = 0.39$, $p < 0.01$) and peak activity (measured by actimetry) ($n = 36$, $r = 0.43$, $p < 0.01$), in these groups. In the anxiety group, drive to exercise correlated with self-reported vigorous activity only ($n = 28$, $r = 0.65$, $p < 0.01$).

Across the groups, drive to exercise correlated (moderately) with EDE-Q global score ($n = 107$, $r = 0.48$, $p < 0.01$), poorly with the DASS anxiety score ($n = 107$, $r = 0.23$, $p < 0.02$) and with BMI, there was an inverse correlation ($n = 107$, $r = -0.38$, $p < 0.01$) It was also correlated with exercising to control weight ($n = 105$, $r = 0.5$, $p < 0.01$), to improve tone ($n = 102$, $r = 0.40$, $p < 0.01$), to improve mood ($n = 101$, $r = 0.49$, $p < 0.01$) and for fitness ($n = 101$, $r = 0.3$, $p < 0.01$).

When the two AN groups were combined, drive to exercise was highly correlated with exercising to improve mood ($n = 46$, $r = 0.74$, $p < 0.01$), for fitness ($n = 46$, $r = 0.54$, $p < 0.01$), to control weight ($n = 50$, $r = 0.55$, $p < 0.01$), to improve tone ($n = 47$, $r = 0.44$, $p < 0.01$), and for health ($n = 47$, $r = 0.43$, $p < 0.0$). In the anxiety group, drive to exercise correlated with exercising to improve mood ($n = 28$, $r = 0.44$, $p < 0.02$). Lastly, in the HCs, drive to exercise was not significantly correlated with other measures.

Multivariate models predicting drive to exercise

Hierarchical multiple regression was conducted to examine the extent to which ED pathology, anxiety, depression, stress and REI sub-scales predicted drive to exercise, (after

controlling for percentage muscle and BMI). Across the groups, BMI and muscle (%) were entered at Step 1, and explain roughly 15% of the variance in drive to exercise. When REI and DASS sub-scale scores and global EDE-Q score, were entered (Step 2), the total variance explained by the model was 57% ($p < 0.01$). Variables entered at Step 2, explained an additional 41.6% of the variance in drive to exercise, after BMI and muscle (%) had been controlled for. In the final model, those variables that contributed most to the overall variance in drive to exercise were: exercising to improve mood (6.3%, $p < 0.01$), exercising for weight control (4.9%, $p < 0.01$) and global EDE-Q score (3.6%, $p < 0.01$).

Following the above, the analysis was repeated for each group. In HCs, DASS and REI sub-scale scores and the global EDE-Q score, explained roughly 35% of the variance in drive to exercise, but overall, the model was not significant ($p = 0.74$). In the group with anxiety symptoms, these variables explained roughly70% of the variance [after controlling for BMI and muscle(%)]: the overall model was significant ($F(11) = 5.54$, $p < 0.01$). Specifically, stress (DASS sub-scale) contributed the most to the variance in drive to exercise (18%, $p < 0.01$) together with exercising to improve mood (11%, $p < 0.01$) and global EDE-Q score (8%, $p < 0.05$). For the outpatient AN group, DASS and REI sub-scales and the global EDE-Q score, explained 86% of the variance in drive to exercise, (after controlling for BMI and muscle [%]) ($F(11) = 10.48$, $p < 0.01$). In this group, exercising to improve mood and ED psychopathology contributed the most to the variance in drive to exercise (EDE-Q: 25%, $p < 0.01$; REI-mood: 27%, $p < 0.01$). Other significant contributions were made by exercising to improve tone (10%, $p < 0.01$), stress (12%, $p < 0.01$), and exercising for health (8%, $p < 0.01$).

The analysis was repeated using self-reported (IPAQ) and objective (actimetry) measures of PA as dependent variables: the resulting models were not significant.

Longitudinal studies related to PA

We also investigated PA longitudinally over 24 weeks in patients with AN. The four groups of participants were the same and the methodology was similar to that used in the cross-sectional study. PA was measured continuously for 8 weeks and at follow-up (weeks 12 and 24) by actimetry and self report (IPAQ). Measures of general and ED related psychopathology were made in parallel.

ED psychopathology and physiological measures remained consistent with diagnosis. Drive to exercise, depression, stress and anxiety were, as might have been predicted, consistently higher in the two AN groups compared to the HC and the group with anxiety symptoms: highest values were seen in the inpatient AN group. In all four groups, there was a wide range in activity, especially on the self report (IPAC) scores but mean actimetry values were relatively constant over time. In AN (compared to HC and the group with anxiety symptoms), self-reported activity was higher on measures of total, walking and moderate PA. In the two AN groups, the drive to exercise was correlated with self-reported exercise. The objective measures (actimetry) showed no statistically significant difference in levels of PA between the four groups.

The data arising from the longitudinal study are in agreement with the results from the cross-sectional investigation. For example, comparison of the objective and the self report data suggests that in in the AN groups, self- reported overactivity is perceived rather than real and may arise from factors such as drive to exercise. It is also of note that levels of activity remain relatively constant across the duration of the study. Furthermore, the objective data suggest that levels of PA do not differ between the AN groups and the HC. What is perhaps surprising is that levels of activity are not apparently decreased by being in an inpatient setting, where limits on activity may have been set. This may be because people in an inpatient setting spend considrable time walking (eg pacing). It suggests that levels of PA are difficult to regulate in severely ill patients where there is a high drive to exercise. However, given that some of the patients have a very low BMI and high levels of ED pathology, diminished fat reserves and a loss of muscle tissue (i.e. the AN-IP group), this relatively "normal" level of activity may be of some clinical concern and should be considered. In this respect, it should also be seen in the context, of setting a balance which recognises the beneficial effects of exercise on mood and anxiety and its effects on bone health, energy expenditure and PA.

Energy expenditure and physical activity

A final element of the study was an investigation of energy expenditure (EE) asociated with PA in AN. The data was derived from the measures of self reported activity and from physiological measures such as BMI. PA related EE was estimated by converting IPAQ scores to "metabolic equivalent of task" values (MET) and then to corrected MET (cMET), to adjust for differences in resting metabolic rate (RMR).

Compared to the healthy control group, RMR was lower in the outpatient group (by 11%) and in the inpatient group (by 17%). When EE is corrected for RMR, (cMET), no group differences in EE emerged. We estimate that EE (ie energy expenditure due to PA) is roughly360 kcal/day in the outpatient group and 400 kcal/day in the inpatient group. Based on the use of the self report (IPAQ), data, combining RMR with EE provides energy neutral points of 1620 kcal/day for the outpatient AN group and 1578 kcal/day for the inpatient AN group. Because the two patient groups report that they undertake higher levels of exercise than that obtained from the objective actimetry scores, the actual total daily energy expenditure in these two clinical groups is likely to be lower than our estimate (eg. by roughly 200kcals/day).

EE may be of concern when a patient is at low weight/ not eating. However, given they have a high drive to exercise and that PA may improve affect, reduce stress and possibly improve general health, it is arguable that awareness of the caloric consequences of exercising, will enable the desire to exercise to be more easily negotiated in relation to food intake.

Discussion

Summary

The data on psychopathology and on body composition were as expected ie patient groups had significantly higher ED pathology, anxiety, depression and stress and lower BMI, fat and muscle than the HC and the anxiety groups. This information was fairly consistent both cross sectionally and longitudinally.

The PA data is less easy to interpret. Self-reported PA, (IPAQ scores), showed that the two AN groups reported higher levels of time across all levels of PA (especially walking) , compared to the anxious and HC groups. These two patient groups reported slightly different exercise profiles: AN-OP reported undertaking more moderate and vigorous activity that the two control groups and the AN-IP reported the opposite, ie that they engaged in less moderate and vigorous activity than HCs. In contrast, , the actimetry showed that the AN groups had quite similar average and peak PA levels as those reported by the HC and anxious participants.

Both the groups with AN had significantly higher drives to exercise than the HCs and the anxious group and the groups valued different reasons for exercising as more or less

important. For example, the AN groups rated weight control, improving mood and improving tone as more important motivators for engaging in exercise. In contrast, the anxiety and HC groups rated health as the most important exercise motivator.

Physical activity (PA)

PA measured by actimetry (both cross sectionally and longitudinally) shows that the AN groups spent similar amounts of time exercising and at similar intensities as HC, whereas, on the self report measure, the outpatient AN group have higher PA scores at all intensity levels. The self-report data are therefore consistent with other findings indicating increased of PA in AN (230, 233, 234) and also with our first hypothesis. The objective data do not support our original hypothesis, but do support the findings of Zipfel and colleagues that individuals with AN and controls showed similar levels of PA when objective measures are used (egthe doubly labelled water method). Zipfel et al also reported that not all individuals e with AN have increased levels of PA (271). However, In the present study, however, although we saw arange in activity in the AN group, there was no relationships, with, for ex., between illness severity and PA and lastly, no evidence of activity based sub-groups emerged.

The data from the self report (IPAQ) measure (both cross sectional and longitudinal) suggest that there are group differences in the exercise type that is undertaken e.g. inpatients reported spending significantly more time walking. This suggests that these individuals choose types of exercise that are appropriate for their weight and physical ability in order to satisfy their high drive for exercise: it may also be that it is the most feasible method in an inpatient setting

Several potential explanations can be provided for the differences between subjective and objective measures of PA. For example, objective measures, may not accurately detect different intensities or types of PA. This could occur where arm movements may not be consistent with the intensity of activity e.g. uphill walking or cycling. There may also be some limitations to self-report measures in terms of recall accuracy. Additionally, it is possible that different groups estimate their levels of PA differently. HC participants may underestimate this while, conversely, individuals with AN, may perceive themselves to be highly active. Furthermore, in AN patients who are physically compromised, PA at any level may be seen by them as a significant physical investment and this may result in them overestimating their activity. This idea is consistent with the observed large *SD* and variance in our IPAQ data. Overall, the results suggest that individuals when they are ill (and

possibly in an inpatient setting) are undertaking in PA at roughly the same level as healthy controls and this in itself is of some clinical concern.

Drive to exercise and PA

Consistent with our second hypothesis, both the AN-IP and AN-OP groups had significantly higher drives to exercise than the HC and the anxiety groups. Secondly, drive to exercise was not different between the HC and the anxious groups. It is therefore suggested that this drive to exercise is more linked to the ED rather than to anxiety. Absence of a strong relationship between anxiety and the drive to exercise or objective/subjective measures of PA further supports thisAcross the whole sample, there was a moderate correlation between drive to exercise and with all measures of self-reported PA ie with total, walking, moderate and vigorous activity. There were also moderate correlations between drive to exercise and global ED score, exercising to to improve mood, improve tone, ,for fitness and for weight control. Lastly, drive to exercise was inversely correlated with BMI and poorly with the DASS anxiety score.

In the AN-IP and AN-OP groups, there was a significant relationship between drive to exercise and exercising to control weight, to improve mood, to improve tone, for fitness and health and peak activity (based on actimetry. In the group with anxiety symptoms, , drive to exercise highly correlated with self-reported vigorous activity. Lastly, drive to exercise was moderately correlated with exercising to improve mood in this group.

Hierarchical multiple regression analysis showed that the global EDE-Q score, exercising to to control weight and to improve mood, predicted drive to exercise across the whole sample after controlling for muscle (%) and for BMI . In the anxiety group alone, stress (DASS sub-scale) contributed most to the variance in drive to exercise. For the AN-OP group outpatients, the biggest contributors to variance in drive to exercise were exercising to improve mood and global EDE-Q score .

Overall, results show that PA has several pychoplogical drivers, as well as exercising to improve fitness and tone. Engaging in PA seems to be driven by the desire to cope with stress and to improve mood in the anxiety group. However, in people with AN, the drive may partly be to improve mood, but in this group, the absence of a relationship between PA and anxiety scores suggests that drive to exercise is not primarily a response to anxiety. It appears that these behaviours are associated with body and weight concerns ie central

elements of ED psychopathology. Data thus support our hypotheses and previous findings (240) that the drive to exercise in AN is substantially motivated by concerns at the core of ED psychopathology, e.g. the cognitive issues related to losing/ maintaining low weight.

Endocrine Findings

AN inpatients have significantly higher cortisol levels than HCs, which is to be expected given the higher level of anxiety in this group. A small correlation was observed between cortisol level and DASS anxiety score. Both AN groups had significantly lower leptin levels than HCs and, there was a strong and highly significant correlation between leptin and body fat percentage (both these findings are consistent with expectations).

Strengths and limitations

A strength of this investigation is that it allowed for PA to be directly compared in people with anorexia nervosa and with moderate anxiety. Secondly, participants in each groups were of similar ages, which is important when comparing PA. Additionally, combining both objective and subjective measures allowed us to assess and compare different methodologies for studying PA. An additional advantage was that measures of eating disorder psychopathology, general pychopathology and biology were collected along with the activity data. Finally, the study was conducted cross sectionally and longitudinally (over 24 weeks).

The investigation had some limitations in that missing data resulting from participants occasionally forgetting to put on the actiwatches and also due to the collection of retrospective self-report data over a period of 7 days, which may be slightly less reliable. In addition, there is the possibility of some recruitment bias in the AN groups i.e. not all of the people with the problem might be willing to join an investigation assessing PA. Lastly, participants were predominantly white females and therefore it might not be possible to generalise our data to men and/or to different ethnic groups.

Conclusions

Our activity measurements gathered from self report data indicates that people with AN have higher levels of PA than HCs or than those of a group with moderate anxiety, while the actimetry data shows these groups do not differ in their amount or level of PA. It is possible that self-report overestimates the level of PA in AN due to differences in perception caused by the ED or because the group are in poor physical health. Findings also show patients with AN have a higher drive to exercise than HC and anxiety groups. In AN patients, eating

disorder pathology, rather than anxiety, appears to be a more important contributor to their increased drive to exercise. Estimates of RMR and of energy expenditure arising from PA, will inform decisions related to the clinical management of people with anorexia nervosa and will also inform discussions on the role and use of exercise programmes in treatment

Chapter 8. Preventing deterioration and relapse in severe anorexia nervosa: Randomised controlled feasibility trial of an e-mail guided manual-based self-care programme based on the Maudsley Model of Anorexia Nervosa Treatment for Adults (WP5)

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Abstract

Word count: 250

Background: Relapse rates after inpatient treatment of anorexia nervosa (AN) are high. The aims of this study were (a) to assess the feasibility of a relapse prevention programme for people with AN; (b) to acquire information to inform a large randomised controlled trial (RCT) of this intervention.

Methods: Participants were inpatients with AN, aged 16 or above. Participants were recruited from seven UK specialist eating disorders units and randomly allocated to receive either manual-based e-mail guided self-care for twelve months combined with treatment as usual (TAU) or TAU alone. The manual was based on the Maudsley Model of Anorexia Nervosa Treatment for Adults (MANTRA). E-mail support was delivered weekly by therapists. Outcome assessments included body mass index, Eating Disorders Examination, depression, anxiety, quality of life and service utilisation at 6 and 12 months post-randomisation. Treatment effect sizes (Cohen's d) were calculated.

Results: 41 patients participated. At 6 months post-randomisation (and post-discharge) there was little difference between groups, with effect sizes between $d = -0.08$ and $d = 0.3$. At 12 months, patients receiving the experimental intervention had a higher BMI ($d = 0.41$) and lower scores on the Depression, Anxiety and Stress Scale ($d = 0.64$). Readmission rates were 5/22 (22.7%) in the experimental group and 5/16 (31.2%) in the TAU alone group. No harms were detected.

Conclusions: These findings suggest that this low-intensity relapse prevention may be beneficial in the aftercare of inpatients with ANand that a large-scale RCT of this intervention may be justified.

Trial Registration number: ISRCTN18274621

<u>Introduction</u>

Anorexia nervosa (AN) is a life-threatening illness with a mortality rate twice that of other psychiatric inpatients, and a suicide rate 200 times that of the general population (67, 272, 273). There are high levels of physical disability and psychological comorbidity and the median duration of AN is six years (274). Whilst for most patients with AN the treatment of choice is outpatient psychological therapy, a proportion of cases with severe and potentially life-threatening illness need skilled refeeding in hospital. The threshold for inpatient treatment in AN differs in different countries. In continental Europe, admission to hospital appears to be more common than in the UK where this treatment is reserved for the most severe cases. Duration of inpatient care also varies in different health care systems with longer durations of admissions in European countries than in the USA (191). Whilst patients usually manage to gain weight in hospital, deterioration and relapse following inpatient treatment is common and typically occurs within the first year of treatment. Approximately 30-50% of those who remit relapse (226, 275-278). The reasons for these high relapse rates are complex, but may in part be to do with patients' physical improvements during inpatient refeeding not being mirrored by similar psychological improvements. Thus effective psychological aftercare following inpatient treatment is important. This is echoed by the NICE guidelines for Eating Disorders (279) which recommend that people discharged from inpatient care should be followed up for at least one year post-discharge. In practice, as patients often live at some distance from a specialist inpatient unit this follow-up often is delivered by non-specialists, making after-care practice variable and haphazard.

Only a handful of studies have addressed the question of *how* best to reduce relapse rates after inpatient weight restoration. Antidepressant treatment alone appears to be unacceptable to the majority of eligible patients (280, 281) and ineffective (204). Two studies in adolescents found family therapy to be superior to individual treatment (188, 282) or treatment as usual (283). Conversely, in adults with AN, one study found individual therapy to be somewhat superior to family therapy in preventing relapse (188, 282) although a second study using a similar design found no difference between family therapy and two types of individual therapy (284). In one small study, cognitive behavioural therapy (CBT) was superior to nutritional treatment alone in preventing relapse (205). However, in another study which compared CBT alone or in combination with fluoxetine alone, drop-out rates in all three groups were too high to draw any conclusions about efficacy (281), casting doubt on the acceptability of these interventions. Finally, a large scale randomised controlled trial (RCT)

(n = 258 participants) from Germany compared an internet-based cognitive-behavioural relapse prevention programme with treatment as usual. In the intention-to-treat analysis patients receiving the internet-based relapse prevention programme gained a small amount of weight, whereas those receiving treatment as usual, lost a small amount, but the difference was non-significant. There were significantly more readmissions to hospital in the relapse prevention group (285).

We have designed and piloted a novel manual-based outpatient treatment for adults with AN (MANTRA, Maudsley Model of Anorexia Nervosa Treatment for Adults) (19, 125). The content, structure, research underpinning this treatment and iterative development process have been described in detail elsewhere (20, 135, 286). In brief, MANTRA is an empirically-based cognitive-interpersonal treatment, which is trait-focused and targets key intra- and interpersonal maintenance factors of AN. It is centred around a patient-manual and is modularized with a clear hierarchy of procedures, tailored to the needs of the individual. It has shown promise in pilot studies (135, 286). For the purpose of the present study this treatment and manual were adapted for use in inpatients following discharge from hospital. We evaluated here the feasibility of using it as an internet-based guided self-care treatment, supported via email, given that many patients live at a considerable distance from specialist eating disorder units (iMANTRA).

The aims of the study were (a) to assess the feasibility of using e-mail guided self-care treatment added to treatment as usual (TAU) in the post-admission care of hospitalised AN patients and (b) to acquire key information that would inform development of a large-scale RCT that will assess the efficacy, cost and cost-effectiveness of this intervention added to treatment as usual (TAU) compared to TAU alone.

The specific objectives of the proposed feasibility study were to:

a. assess recruitment and treatment uptake rates.
b. determine what is an appropriate frequency of email support for patients.
c. determine the best instruments for measuring outcomes in a full trial by examining the quality, completeness, and variability in the data.
d. estimate the treatment effect sizes and standard deviations for outcome measures to inform the sample size calculations for a large-scale RCT.

e. evaluate whether the treatment is operating as designed by analysing process measures, such as worry and intolerance of uncertainty.

f. determine whether patients with AN see this treatment as acceptable and credible.

Method

Design

The trial was a multi-center two-arm feasibility trial which compared iMANTRA added to TAU with TAU alone in consecutive referrals of patients discharged from inpatient treatment for anorexia nervosa. Ethical approval was obtained from the National Research Ethics Committee (NRES) West Midlands – Edgbaston, reference number: 08/H1208/33. The trial was registered with Current Controlled Trials: ISRCTN18274621. Recruitment and follow up procedures took place between March 2009 up until December 2012.

Participants and recruitment

Patients were recruited from seven specialist adult or adolescent inpatient units in the UK. These were: South London and Maudsley NHS Foundation Trust; Seacroft Eating Disorders Unit, Leeds Teaching Hospitals NHS Trust; St Ann's Hospital, Barnet, Enfield and Haringey Mental Health Trust; South West London and St George's Mental Health NHS Trust; Huntercombe Hospitals (Stafford, Edinburgh); The Priory Hospital, Roehampton, Royal Victoria Hospital, Newcastle. Patients' suitability for participation in the study was checked by a clinician from the eating disorders team towards the end of their inpatient treatment (i.e. within 1-month of discharge). If the patient was suitable for participation, their fully informed written consent was sought and after this she/he was introduced to the researcher who completed the research assessment.

Inclusion/exclusion criteria

Inclusion criteria

Patients fulfilling criteria for DSM-IV anorexia nervosa or atypical anorexia nervosa who had undergone a period of inpatient treatment in one of the participating Eating Disorders Services were eligible for inclusion in the study if they: were aged 16 years or over; had reliable access to broadband internet; were available over the full duration of the study; had shown clinically significant weight gain during inpatient treatment (a minimum of approx. 3 kg or 1 BMI point).

Exclusion criteria

Unstable AN, i.e. actively losing weight at the end of treatment, insufficient knowledge of English or literacy levels insufficient to allow understanding of the manual and assessment, psychosis, acute suicidality, substance dependence, or diabetes mellitus. We did not exclude patients on psychotropic medication (antidepressants, antipsychotics) which are commonly prescribed in this population.

Comparison Groups

Common features

All participants were signed up for regular weighing and physical risk monitoring at their GP surgery. A crisis plan with names and numbers of who to contact in an emergency was also drawn up with patients prior to discharge.

(a) Internet-based MANTRA plus TAU

Those allocated to iMANTRA plus TAU were sent an email informing them of their treatment allocation and giving them some information about their email therapist and the frequency and nature of the email contact. E-mail contact was offered one to three times weekly for the first 6 months following discharge and then more flexibly (once weekly to monthly) during months 7 to 12. Participants were also told not to use their email therapist for urgent out-of-hours or other crisis support and instead use the crisis contacts on their list. Participants were asked to complete an online questionnaire giving some background information about themselves, to help their email therapist to get to know them better. This questionnaire included questions on their current difficulties, struggles and worries and their hopes, ambitions and goals for the future; their key current relationships, in particular with people who might be able to support them, their personal history and any important events that have affected or shaped them and any previous treatments that they may have had (a copy of this questionnaire can on request be obtained from the authors).

Patients were also offered an initial phone call with their online therapist to give both patient and therapist the opportunity to ask questions and clarify information. Finally, patients were sent the revised version of the MANTRA workbook. This included: (a) a traffic light system of relapse risk for patients to complete, to increase their awareness of potential indicators of such risk, (b) a nutrition plan that was designed for weight maintenance and also gave information on what to do if more weight gain was needed, (c) a module addressing anxiety-

related processes, such as worry and intolerance of uncertainty and strategies to reduce them; (this was included as patients with anorexia generally have high levels of anxiety, worry and intolerance of uncertainty (287-290), and it was thought that during the post-discharge period this would be particularly intensive and a therefore an important treatment target); (d) and strategies to prevent and cope with deterioration and lapses.

The role of the therapist was to be motivational and supportive, with the aim to guide patients in their use of the workbook, by suggesting use of relevant modules, thereby tailoring the intervention to the relapse risk and clinical profile of the patient. Patients in this group also received TAU from their local Community Mental Health Team or Child and Adolescent Mental Health Team.

(b) Treatment as Usual (TAU)

Patients randomised to this group did not receive the internet-based intervention. They received treatment as usual from their local Community Mental Health Team or Child and Adolescent Mental Health Team. They were followed up at regular intervals using the same assessment measures as patients who received the iMANTRA-intervention.

Measures

Body Mass Index (BMI)

BMI (weight/height^2) was obtained from the medical notes for each patient at admission and at discharge. At 6-months and 12 months this was obtained from treating clinicians or from patient self-report.

Interview measures

These were done at baseline, 6 months and 12 months and included: (a) the Eating Disorders Examination (EDE, 291) and (b) the Client Services Receipt Interview (CSRI, 152). These were completed in person or by telephone.

The EDE is a widely used, semi-structured interview that generates 4 subscale scores: dietary restraint, eating concern, weight concern and shape concern. The mean of these 4 subscales is used to create a global score.

The Client Services Receipt Interview (CSRI) is an inventory of service use which facilitates estimation of support costs. It was adapted for the current study to cover a wide variety of

hospital, mental health, and community-based services as well as medications, impact of employment and additional personal expenditure due to the eating disorder.

Questionnaire measures

These were completed at baseline, 6 and 12 months.

Eating disorders pathology

Eating Disorders Examination-Questionnaire: EDE-Q; Fairburn & Beglin, 1994): This is a self-report measure assessing eating disorder symptoms over the previous 28 days. This instrument has good reliability and validity in ED samples (211). High scores indicate greater eating disorder psychopathology.

Other psychopathology

Depression, Anxiety and Stress Scale (DASS) –Short Version (95): This is a 21-item self-report measure to assess mood state over the past seven days using a 4-point Likert scale. Total score as a measure of general distress or depression, anxiety and stress subscales can be used. High scores indicate higher symptomatology. This measure has good reliability and validity (209).

Quality of life

World Health Organisation Quality of Life –brief version (212): Items are rated on a 5-point Likert scale pooled in four domains: physical health, psychological, social relationships and environment. Good psychometric data have been reported for this scale. High scores indicate better quality of life.

Anxiety related processes

Penn State Worry Questionnaire (PSWQ, 292): This is a 16-item questionnaire rated on a 5-point scale, with higher scores indicating a greater tendency to worry. The PSWQ has very good psychometric properties (for review see 293) and is the most established measure of trait worry.

Intolerance of Uncertainty Scale (IUS, 294): The IUS is a 27-item measure designed to assess the cognitive, emotional and behavioural aspects of intolerance of uncertainty (IU). Items are scored on a five-point Likert scale. High scores denote high levels of IU. The IUS has very good psychometric properties (295).

Randomisation, blinding and protection against bias

Randomisation was conducted independently from the trial team by the King's Clinical Trials Unit using a computerised system. Patients were randomised to the i-MANTRA intervention plus TAU versus TAU alone, at a ratio of 1:1. Randomisation was carried out using minimisation to balance groups for prognostic factors (previous hospitalisation; illness subtype). Patients were told about the outcome of randomisation by email sent to them by a study administrator. Throughout the trial every effort will be made to ensure that the researcher who conducted outcome assessments remained blind to patients' treatment allocation.

Therapists

Three experienced eating disorder therapists delivered the email support. All had undergone a one day training programme preparing them to deliver the intervention. The focus of the training was to standardise delivery of the email contact. Therapists were instructed to keep emails brief, be informal, warm and supportive in tone, point patients in the direction of appropriate materials from their manual that might be relevant in keeping them well or helping them to make further improvement and provide non-intrusive monitoring of symptoms via the traffic light relapse prevention tool.
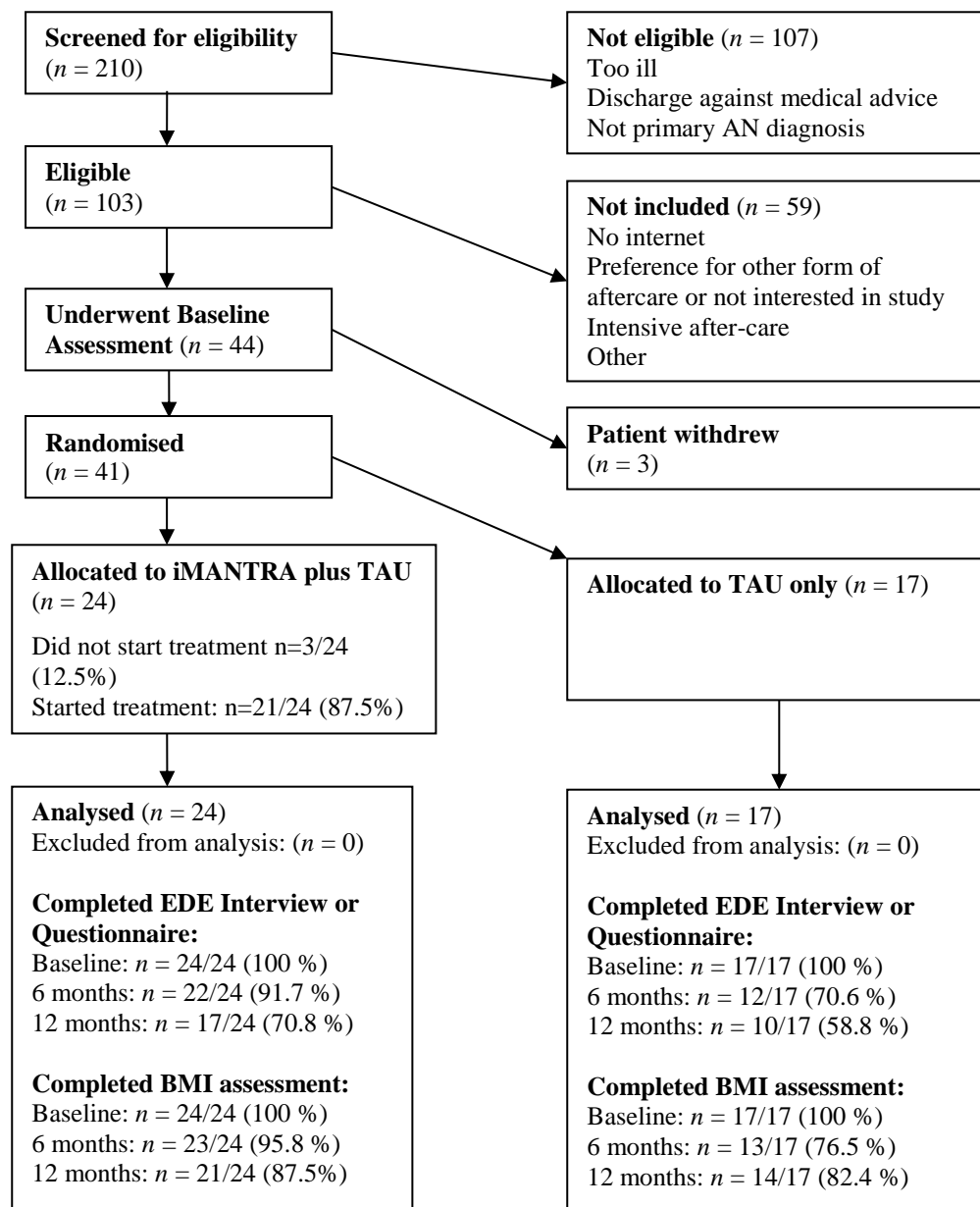
Statistical analyses

Outcomes were analyzed on an intention-to-treat (ITT) basis, that is, participants were analyzed in the group to which they were randomized irrespective of their compliance with the assigned treatment. No formal hypothesis testing was undertaken, as this is a feasibility study. Effect sizes (Cohen's d) were calculated for continuous outcomes at 6 and 12 months from means, standard deviations and sample sizes using the effect size calculator of the Campbell Collaboration (www.campbellcollaboration.org/resources/effect_size_input.php).

Results

Patient flow

Figure 4 shows the participant flow through the study. Twenty-four participants were randomised to iMANTRA plus TAU and 17 to TAU alone.

Screened for eligibility (*n* = 210)	→	**Not eligible** (*n* = 107) Too ill Discharge against medical advice Not primary AN diagnosis

Screened for eligibility
(*n* = 210)

Not eligible (*n* = 107)
Too ill
Discharge against medical advice
Not primary AN diagnosis

Eligible
(*n* = 103)

Not included (*n* = 59)
No internet
Preference for other form of
aftercare or not interested in study
Intensive after-care
Other

Underwent Baseline Assessment (*n* = 44)

Patient withdrew
(*n* = 3)

Randomised
(*n* = 41)

Allocated to iMANTRA plus TAU
(*n* = 24)

Did not start treatment n=3/24
(12.5%)
Started treatment: n=21/24 (87.5%)

Allocated to TAU only (*n* = 17)

Analysed (*n* = 24)
Excluded from analysis: (*n* = 0)

Completed EDE Interview or Questionnaire:
Baseline: *n* = 24/24 (100 %)
6 months: *n* = 22/24 (91.7 %)
12 months: *n* = 17/24 (70.8 %)

Completed BMI assessment:
Baseline: *n* = 24/24 (100 %)
6 months: *n* = 23/24 (95.8 %)
12 months: *n* = 21/24 (87.5%)

Analysed (*n* = 17)
Excluded from analysis: (*n* = 0)

Completed EDE Interview or Questionnaire:
Baseline: *n* = 17/17 (100 %)
6 months: *n* = 12/17 (70.6 %)
12 months: *n* = 10/17 (58.8 %)

Completed BMI assessment:
Baseline: *n* = 17/17 (100 %)
6 months: *n* = 13/17 (76.5 %)
12 months: *n* = 14/17 (82.4 %)

Figure 4: CONSORT flow diagram (WP5)

Patient characteristics at baseline

Patients in the two treatment groups were similar in terms of baseline socio-demographic and clinical characteristics (see *Table 27*) with the exception of the WHOQOL Environmental subscale where the iMANTRA group had significantly poorer quality of life than the TAU group ($t(32.6) = -2.34$, $p = 0.025$). All had severe AN (mean admission BMI 14.1 kg/m^2) with just over half (51%) having had at least one additional previous admission to hospital. Patients had made considerable gains in weight whilst in hospital (discharge BMI 18.0kg/m^2) and prior to coming into the study.

Acceptability of iMANTRA

21/24 (87.5%) of patients allocated to iMANTRA plus TAU took up this treatment.

Treatment outcomes

Table 28 shows outcomes on interview and questionnaire variables at 6 and 12 months.

At 6 months there was little difference in outcomes between groups, with effect sizes between $d = -0.08$ and $d = 0.3$, i.e. negligible to small. At 12 months, patients receiving the experimental intervention had a higher BMI ($d = 0.41$) and lower total scores on the DASS ($d = 0.64$). However, confidence intervals were wide and overlapped with zero.

Service utilisation

Ten patients required re-admission to hospital during the trial, 22.7% (5/22) in the iMANTRA group and 31.2% (5/16) in the TAU alone group. This difference was not significant ($\chi^2(1) = 0.347$, $p = 0.556$). Comparable numbers of patients in both groups had GP or outpatient care during the study period (iMANTRA: 12/18 (66.6%) and TAU alone: 10/15 (66.6%). The proportion of patients with no additional treatment was also similar in both groups (iMANTRA 1/18 (5.5%) and TAU alone 1/15 (6.6%). No patient died during the study period.

Harms

No harms were detected.

Table 27: Baseline clinical and demographic data

	Whole Group		iMANTRA plus TAU		TAU only	
	n	*m* (*SD*) or *n* (%)	*n*	*m* (*SD*) or *n* (%)	*n*	*m* (*SD*) or *n* (%)
Demographic details						
Age	41	24.2 (9.6)	24	24.8 (10.1)	17	23.3 (8.9)
Gender ratio (m:f)	41	4:37	24	2:22	17	2:15
Proportion with a partner	41	5/41 (12%)	24	4/24 (16.6%)	17	1/17 (6%)
Clinical details						
Diagnosis:	41		24		17	
AN-R		33/41 (80.5%)		20/24 (83.3%)		13/17 (76.5%)
AN-BP		8/41 (19.5%)		4/24 (16.6%)		4/17 (23.5%)
Age of onset	41	17.6 (6.0)	24	17.8 (4.8)	17	17.4 (7.6)
BMI at hospital admission	38	14.1 (1.4)	23	13.9 (1.7)	15	14.3 (1.0)
Proportion with ≥1 previous admissions	41	21/41 (51.2%)	24	12/24 (50%)	17	9/17 (52.9%)
BMI at study entry	41	18.0 (1.9)	24	18.1 (2.2)	17	17.9 (1.4)
EDE global	40	2.8 (1.4)	24	2.9 (1.3)	16	2.7 (1.6)
DASS total score	36	28.6 (18.0)	22	28.7 (17.6)	14	28.3 (19.2)
WHOQOL:	35		21		14	
Physical		47.8 (13.7)		48.0 (10.7)		47.5 (17.7)
Psychological		40.1 (15.7)		37.8 (13.4)		43.4 (18.7)
Social		42.1 (22.3)		37.2 (23.6)		49.5 (18.5)
Environmental		67.2 (19.8)		61.5 (20.8)		75.7 (15.10
PSWQ	36	62.6 (13.5)	22	63.7 (12.0)	14	60.9 (15.8)
IUS	36	87.9 (27.8)	22	88.3 (27.3)	14	87.2 (29.5)
Proportion currently taking psychotropic medication	41	24/41 (58.5%)	24	14/24 (58.3%)	17	10/17 (58.8%)

AN-R: anorexia nervosa restricting type, AN-BP: anorexia nervosa, binge-purge type; EDE: Eating Disorders Examination; DASS: Depression, Anxiety and Stress Questionnaire; WHOQOL: World Health Organisation Quality of Life Questionnaire; PSWQ: Pennn State Worry Questionnaire; IUS: Intolerance of Uncertainty Scale.

Table 28: Outcomes and estimates of treatment effects at 6 and 12 months

	iMANTRA plus TAU		TAU alone		Effect Size	
	n	*m (SD)*	*n*	*m (SD)*	*d*	95% CI
BMI at 6 months	23	17.1 (2.9)	13	17.3 (1.88)	-0.08	-0.76 to 0.60
BMI at 12 months	21	18.0 (3.3)	14	16.9 (1.4)	0.41	-0.28 to 1.09
EDE Global at 6 months	22	2.9 (1.7)	12	2.9 (1.8)	0	-0.70 to 0.70
EDE Global at 12 months	17	2.9 (1.7)	10	2.9 (1.9)	0	-0.78 to 0.78
DASS Total at 6 months	18	28.6 (16.9)	9	26.6 (20.4)	0.11	-0.69 to 0.91
DASS Total at 12 months	15	26.5 (16.4)	6	37.8 (20.7)	-0.64	-1.61 to 0.33
WHOQOL at 6 months	17		8			
Physical		46.5 (14.8)		43.9 (21.7)	0.15	-0.69 to 0.99
Psychological		39.4 (16.9)		41.6 (20.5)	-0.12	-0.96 to 0.71
Social		42.4 (25.3)		39.9 (18.3)	0.10	-0.73 to 0.95
Environmental		61.6 (22.1)		63.5 (15.3)	-0.09	-0.93 to 0.75
WHOQOL at 12 months	15		8			
Physical		47.5 (16.7)		52.1 (20.6)	-0.25	-1.12 to 0.61
Psychological		39.3 (19.8)		32.1 (25.1)	0.33	-0.53 to 1.20
Social		41.7 (26.4)		46.9 (30.2)	-0.19	-1.05 to 0.67
Environmental		67.2 (20.5)		66.6 (17.2)	0.03	-0.83 to 0.89
PSWQ at 6 months	19	63.2 (11.1)	9	59.3 (15.2)	0.31	-0.51 to 1.15
PSWQ at 12 months	15	62.5 (11.6)	8	59.9 (14.7)	0.20	-0.66 to 1.06
IUS at 6 months	18	91.4 (25.5)	9	87.4 (27.5)	0.15	-0.65 to 0.95
IUS at 12 months	12	88.3 (30.2)	8	95.3 (29.8)	-0.23	-1.13 to 0.66

Discussion

This study shows that iMANTRA is a feasible and acceptable intervention when added to TAU in the post-hospitalisation aftercare of patients with AN. Whilst at 6 months post-admission there was little difference in outcomes (with effect sizes negligible or small), at 12-months between-groups effect sizes favoured iMANTRA in terms of its effects on BMI and depression, anxiety and stress (*d* = 0.4 to 0.6). Moreover, readmission rates were somewhat

lower in the iMANTRA group. Taken together these findings suggest that this approach has promise and should be studied further. Further evidence supporting this approach comes from a study in Germany (296) adapted the MANTRA relapse prevention manual for a brief post-admission aftercare intervention with patient and therapist communicating via telemedicine. In an uncontrolled pilot study, this intervention showed promise (Giel, personal communication).

Given the need for regular physical health monitoring in cases of AN, it has previously been said that self-help treatments are contra-indicated in this condition (297). Our findings show that there were no severe untoward events, suggesting that if delivered with appropriate physical risk monitoring in place, a specialist intervention given at a distance can be delivered safely as an adjunct to TAU.

Clearly, this intervention is not for everyone, as only 19.5% of inpatients screened for the study were found eligible and agreed to participation. This raises the question as to how representative of the typical inpatient population in the UK participants were. A recent multi-centre cohort study of short-term outcomes of hospital treatment of anorexia nervosa in the UK found a mean admission BMI of 14 kg/m^2, a mean discharge BMI of 17.3 kg/m^2, and a mean illness duration of 8 years for adults (218). This suggests that our case mix was very similar to that of a typical adult inpatient with AN.

One important question is how do findings from the present study compare with those of the only other (large-scale) study of internet-based aftercare following inpatient treatment (285). Like the patients in the present study, those in the Fichter study (285) were highly selected, i.e. 1802 patients were screened and 258 of these entered the study (14.3%). Age at entry into the study was very similar in Fichter's to our study, as was patients' BMI at discharge (i.e. study baseline). However, no information is available whether Fichter's patients were as chronically ill or had been as unwell (in terms of their weight at admission) prior to starting treatment.

One important lesson for a potential future study utilising this approach concerns the fact that patients did not know their email therapist. Informal feedback from trial therapists was that this made it harder for patients and therapists to form a therapeutic relationship. In future studies it would be desirable for therapists to meet the patients that they are providing

iMANTRA to, and perhaps this could even be the therapist the patient had worked with in the inpatient unit.

Strengths

The study recruited patients from a range of specialist units in the UK including those in the NHS and private sector and the patients recruited seemed representative of a typical AN inpatient population.

Limitations

The sample size was small and TAU only patients were harder to follow up than those allocated to iMANTRA. This may reflect TAU only patients' disappointment about not being offered the experimental treatment component. No attempt was made to standardise TAU.

In conclusion, this study shows that a low intensity e-mail guided manual-based self-care intervention has promise in reducing deterioration and relapse in the year following inpatient treatment in patients with severe anorexia nervosa.

Chapter 9. Maternal eating disorders: effects on fertility and child development (WP6)

Abigail Easter, Janet Treasure & Nadia Micali

Abstract

Word count: 247

Objectives: Three studies examining the effects of maternal eating disorders (ED) on (1) fertility, and (2) their offspring's dietary patterns and (3) growth trajectories.

Design: Data from the Avon Longitudinal Study of Parents and Children (ALSPAC).

Participants: 11,088 women from the ALSPAC birth cohort and their children.

Main outcome measures: (1) Maternal self-report on time taken to conceive and whether they had ever received help to conceive; (2) maternal report of child diet at 38, 54, 81 and 103 months; and (3) child weight and height at 1, 2, 5 and 10 years.

Results: (1) Women with anorexia nervosa (AN) were more likely than women without ED to have sought fertility treatment and to have had an unintentional pregnancy; women with AN and bulimia nervosa (AN+BN) were more likely than women without ED to have received help to conceive and to have taken longer than 6 months to conceive. (2) Children of mothers with AN and BN were more likely be 'health conscious' in terms of diet and less likely to have a 'traditional' type of diet. (3) There was a complex pattern of differences in trajectories of height, ponderal index and body mass index in children of women with ED compared to children of healthy controls.

Conclusions: Women with ED experience difficulties in the pre-conception period and show post-natal differences in their diet patterns. Growth trajectories in their children were found. Continuity of care from pre-conception to the post-natal period is paramount for women with ED.

Introduction

Psychiatric illness and parenting

Children of parents with a mental illness have an increased risk of developing psychological disturbances and psychiatric disorders themselves (298, 299).Within the study of eating disorders (ED) the topic of pregnancy and motherhood has only been investigated more recently. Nevertheless, there is evidence that ED can affect parenting ability and have adverse outcomes for their child's development (300). Furthermore, the offspring of mothers with an ED are at an increased risk of developing disordered eating themselves, and as such it has been proposed that a cycle of risk may be occurring, perpetuating ED across generations (301). Gaining a greater understanding of the associations between ED, pregnancy and child development may extend our current understanding of the risk of intergenerational transmission of ED.

Eating disorders and fertility

The presence of an ED can cause significant disruption to a woman's menstrual cycle and impaired fertility has been shown to exist across the spectrum of ED. Women with a history of AN have shown to have higher disturbances in their menses compared to healthy controls (302). Furthermore, this differences have been shown to continue in up to 30% of recovered women (303). Women with a history of bulimia nervosa (BN) or eating disorders not otherwise specified (EDNOS) have also shown to frequently have higher disturbances in their menses (304, 305), even though their body mass is usually within the normal range.

There is not enough research to understand the disturbance that women with ED suffer with regards to their fertility. Past research, based on two small studies of women looking for infertility treatment, found similar prevalence's: 16 to 20% of women seeking infertility treatment met clinical criteria for an ED (255, 306). However, there have also been contradictory reports with regards to long-term follow-up studies. For example, in a paper by Bulik and colleagues, they found that the rates and frequencies of pregnancies in women with AN were similar to healthy controls (307); furthermore, another paper by Crow and colleagues found the same results in women with BN (308). On the other hand, when looking at births in women with AN, the number has been reduced to one third of the expected rate (309).

A better and more precise measure of fertility may be time taken to conceive (310, 311). A majority of women will become pregnant after trying to conceive between three and six

months, with 90% of them, succeeding after 12 months (312). Therefore, and based on the data, infertility has been defined as inability to become pregnant after trying to conceive for a period of 12 months or longer (313), with delays in conceive being a good measure of a range of underlying fertility problems.

Dietary patterns in children of mothers with eating disorders

There is evidence that mothers with ED may find catering for the nutritional needs of their children especially challenging. However, only a small number of studies have examined the impact of a maternal ED on their child's diet. The literature indicates a high risk for feeding difficulties in children of women with ED (314). These difficulties may lead to different nutritional intake in their children and have long-term implications for health and development.

Only one previous study has investigated the dietary intake in children whose mothers have an ED (315); although this study found the diet of the children to be generally unaffected, there was some suggestion that children of women with ED consumed less junk food than children in the control group. However, this particular study has a limitation due to the small sample size, and was drawn from a sample of children at different ages at a single time point. No previous studies have longitudinally investigated dietary patterns and nutritional intake in children of women with ED.

Growth in the offspring of women with ED

Taking into consideration the possibility of an association between maternal ED and their offspring's feeding and eating habits, it is important to also consider the possibility of an association between maternal ED and their offspring's growth.

Maternal ED, particularly AN, at the time of pregnancy are associated with higher risk for foetus growth restriction and small birth weight (316, 317). Conversely, it has recently been reported that women with binge eating disorder (BED) during pregnancy are more likely to deliver babies that are large for gestational age (318). Although preliminary studies have suggested that this children may reach an adequate post-natal growth in favourable environments (319), with others indicating that altered growth patterns may continue throughout infancy and childhood (320).

The large majority of studies in the past have used small samples and included large age ranges, making it difficult to generalise findings. To the best of our knowledge, only one

study has investigated growth in the offspring of mothers with ED in a longitudinal manner, Only one study has longitudinally investigated the growth of the offspring of women with ED, reaching the conclusion that children of women with ED gained less weight at one year compared to healthy controls (321); however, their BMI was similar to those of controls when the children reached the age of ten (322).

Aims

The overall aim of the studies undertaken was to further investigate the effects of maternal ED on fertility, and their offspring dietary patterns and growth trajectories. Three separate studies are outlined to achieve the overall aims. The specific aims of each study are outlined below.

Study 1: Time taken to conceive amongst women with eating disorders

The aim of study 1 was to investigate the length of time taken to conceive and the prevalence of fertility problems and unintentional pregnancies in women with ED, compared to women without ED.

Study 2: Longitudinal dietary patterns in the offspring of mothers with eating disorders

The aim of this study was to explore different dietary patterns amongst children of women with ED, compared to children of women without ED, longitudinally between three and nine years.

Study 3: Growth trajectories in the offspring of mothers with eating disorders

The aim of this study was to study the differences in growth trajectories (between birth and ten years) in children of women with ED, compared to children of women without ED and children of women with other psychiatric disorders, in a large prospective population-based cohort.

Methods

Design and Participants

Data for this study was collected from the Avon Longitudinal Study of Parents and Children (ALSPAC) (323). ALSPAC is a longitudinal birth cohort study, based in Avon, England, which includes all women who were willing to participate and who were due to have a child between the 1st April 1991 and 31st December 1992.

A total of 14,663 women were initially enrolled in the study at 9 weeks gestation. Using postal questionnaires, data was obtained from 14, 472 women. In the current studies we only included singleton live births (12,254) and excluded all women who were missing information on psychiatric history (2,019).

Outcomes and Measures

Eating disorder classification

At 12 weeks gestation women were asked questions regarding recent of past psychiatric problems which included: depression, schizophrenia, alcohol abuse, AN, BN and other disorders. For all three studies women were grouped according to their response to this question.

A total of 171 (1.5%) women responded yes to the question 'have you ever had AN', 199 (1.8%) responded yes to having ever suffered from lifetime BN and another 82 (0.7%) responded yes to both AN and BN; with 10,636 (96%) forming the unexposed group (those who answered negatively to the questions on ED).

In studies one and two women reporting a psychiatric disorder (1,166) other than an ED were excluded from the analysis. To investigate whether differences in childhood growth are specific to maternal ED status this group is included in the analysis as a separate comparison group.

Socio-demographic variables

Highest education, household income, parity and ethnicity were collected via questionnaire from the mothers during pregnancy. Child gender and maternal age were recorded at the time of birth.

Study 1 measures: Time taken to conceive

At 12 weeks women were asked 'if they had ever seen a doctor for infertility problems and if they had received treatment or help to conceive the current pregnancy'. In a later stage, at 18 weeks gestation, they were asked how long it took them to conceive, this was a multiple choice questions with four possible answers: less than 6 months, 6-11 months, 1-3 years and more than 3years. For the current study, we collapsed the four possible answers into two dichotomous variables: less/more than 12 months (to study rates of infertility) and less/more than six months (to study underlying difficulties conceiving). The analysis in the current study were restricted to women who had become pregnant intentionally ($n = 7,694$).

Study 2 measures: Dietary patterns

When the children were 38, 54, 81 and 103 months of age, data was collected from Food Frequency Questionnaires (FFQ) and included in the current study. For ease of reporting these time points will be referred to by the child's approximate age in years; 3, 4, 7 and 9, respectively. Each FFQ contained questions asking about the frequency of consumption of a variety of foods and drinks. The mother, or main carer, indicated how often her child was currently consuming a variety of food items on a scale from one to five. All data were standardised and a Principal Component Analysis (PCA), which is described elsewhere (324-326), was performed on the standardised items.

The PCA yielded three distinct dietary patterns: 1. 'processed', 2. 'health conscious', 3. 'traditional' at each time point. An additional dietary pattern was identified at the age of 3 and was labelled 'snack foods'. For each child, a score was created for each dietary pattern, which is used in the analysis described below to investigate adherence (whereby increasing scores implies greater adherence) to each dietary pattern.

Study 3 measures: Height and adiposity

Birth weight and length were obtained via different measures. From medical records, birth weight was obtained and birth length was obtained by ALSPAC staff shortly after birth. Later height and weight data was obtained through helth visitor recorts, parental reports in questionnaires and research clinic attendances. Objective weight and height were collected from age seven onwards. Ponderal Index (PI) was calculated as weight(kg)/height(m)^3, and Body Mass Index (BMI) was calculated as weight (kg)/height(m)^2.

Statistical analyses

Study 1: Time taken to conceive amongst women with eating disorders

We used univariable and multivariable logistic regressions models to investigate the role of predictors (maternal lifetime ED: AN, BN, AN+BN and no ED) on our main outcome variables. These were: frequency of planned pregnancies, fertility related problems and treatment, time taken to conceive.

Covariates hypothesised as confounders were included at a second stage in analytical models: maternal and paternal age, pre-pregnancy smoking, maternal education level and parity.

Study 2: Longitudinal dietary patterns in the offspring of women with eating disorders

Univariate analysis of variance (ANOVA) and binary logistic regressions were used to assess differences in participant characteristics in groups of women who reported ever having AN, BN and AN+BN, compared with the unexposed group.

Longitudinal analysis of dietary patterns was investigated using linear mixed-effects models, with random intercepts. Predictors were maternal lifetime ED group and the time point at which childhood dietary patterns were assessed (i.e mean time of completion at assessment as a continuous variable). A random intercept was also included in the model to take into account the variance due to individual differences at baseline in dietary patterns. All nutrient data were log-transformed to achieve a normal distribution prior to analysis. Since the dietary pattern 'snacks' was only identified in the three year old children, a linear regression model was used to assess group differences in pattern score. Due to missing data we used a dataset derived from multiple imputations for these analyses.

The models were run unadjusted initially and then adjusted for potential covariates that have been shown to potentially influence outcomes in the same sample: maternal age, education, ethnicity, household income, parity and child gender (326). We were particularly interested in investigating the role of child gender and age on the main outcome variables, therefore group-by-time point and group-by-child gender interaction terms were tested in all models.

All analyses for study one and two were performed using Stata (Version 10 for Windows) and all statistical tests presented are two-tailed.

Study 3: Growth trajectories in the offspring of mothers with eating disorders

Statistical modelling

We modelled individual growth trajectories using multi-level models, including two levels: a time and an individual level in the statistical package MLwiN (327). We used fractional polynomials to identify the curves that best-fit the data. These models allow use of all available data under the assumption of MAR. They model the change in scale and variance of growth over time, and the individual variance in growth trajectories, allowing each individual to have a unique intercept and slope.

Given the complicated patterns of growth in childhood, we used ponderal index-PI (kg/m^3) as the adiposity measure between birth and 2 years. BMI was modelled from 2 to 10 years of age and height from birth to 10 years.

Growth trajectories were modelled by exposure group (maternal lifetime AN, BN and AN+BN). They were estimated by fitting interaction terms between each exposure group and the constant (i.e. PI at birth, length at birth, or BMI at two years of age) and each of the polynomial terms in the multi-level models. This method generates specific average growth trajectories for children in each exposure group. Z-tests were used to determine statistical differences in outcomes, comparing each group to the unexposed group (no maternal ED) at various time-points.

Associations between maternal ED and offspring growth trajectories were investigated in unadjusted and adjusted multi-level models, which included a priori confounders (e.g. maternal education, maternal age, gestational age, and parity).

Given known gender differences in childhood growth, and gender specific effects of maternal lifetime ED, we modelled trajectories separately by gender.

Results

Study 1: Time taken to conceive amongst women with eating disorders

Fertility problems

More women across all four groups had never seen a doctor about treatments for problems with conceiving (n = 9,658, 88.1%), or had used any treatment of help to conceive for this pregnancy (*n* = 10,693, 97.3%). However, women with AN had a higher chance of having seen for fertility problems during lifetime compared to the general population after we adjusted for pertinent covariates. Women with AN+BN were also two times more likely (6.2%) to receive treatment to help them conceive than unexposed women (2.7%). See *Table 35*.

Table 29: Logistic regression of fertility problems and intentional pregnancy

	Unadjusted Models				Adjusted Models		
	AN *n* = 171	BN *n* = 199	AN+BN *n* = 82	General Population *n* = 10, 636	AN *n* = 171	BN *n* = 199	AN+BN *n* = 82
Seen a doctor for fertility problems: *n*(%) OR (95% CI)	35(20.6%) 1.9** (1.3-2.8)	22(11.2%) 0.9 (0.6-1.49)	16(19.5%) 1.8*(1.0-3.1)	1231(11.7%) Ref	1.6* (1.1-2.5)	1.0 (0.6-1.6)	1.9* (1.1-3.4) Ref
Received help to conceive: *n*(%) OR (95% CI)	4 (2.3%) 0.8 (0.3-2.3)	3 (1.5%) 0.5 (0.2-1.8)	5 (6.2%) 2.3§ (0.9-5.8)	287 (2.7%) Ref	0.8 (0.3-2.3)	0.6 (0.2-1.9)	2.4* (0.9-6.3) Ref
Intentional pregnancy: *n(%)* OR (95% CI)	96 (58.5%) 0.5** (0.4-0.8)	131 (67.1%) 0.8 (0.6-1.0)	53 (66.2%) 0.7 (0.5-1.2)	7,414 (71.7%) Ref	0.5** (0.4-0.7)	0.8 (0.6-1.0)	0.7 (0.4-1.1) Ref

*: $p \leq 0.05$, ** $p < 0.001$, § $p = 0.07$ vs. unexposed group. Odds Ratios (OR), 95% Confidence Intervals (CI)

This table is reproduced from: Easter, A., Treasure, J. and Micali, N. (2011), Fertility and prenatal attitudes towards pregnancy in women with eating disorders: results from the Avon Longitudinal Study of Parents and Children. BJOG: An International Journal of Obstetrics & Gynaecology, 118: 1491–1498. doi: 10.1111/j.1471-0528.2011.03077.x

Time taken to conceive

We examined time taken to conceive in our sample. A total of 7,694 women had a planned pregnancy and of those, 74.5% reported having conceived on the first six months. 8.3% took longer than one year and only 3.6% took over three years to conceive. Generally, women in all ED groups reported having taking longer than 12 months to conceive compared women in the general population, and this remained the same for both univariate and adjusted analyses. Women with AN+BN reported having taken longer than six months to become pregnant compared to unexposed women and this difference remained after adjusting for covariates (see Table 36).

Intentional pregnancies

Women with lifetime AN had lower odds of having intentional pregnancies compared to women who were unexposed (41.5% vs. 28.3%). These differences remained after adjusting for relevant covariates.

Table 30: Logistic regression of time taken to conceive

Time Taken To Conceive[1]	Unadjusted OR (95% CI)				Adjusted OR (95% CI)[2]		
	AN $n = 89$	BN $n = 116$	AN+BN $n = 48$	General population $n = 6,883$	AN	BN	AN+BN
Longer than 12 months n (%) OR (95% CI)	14 (15.7%) 1.3 (0.8-2.4)	11 (9.4%) 0.9 (0.5-1.6)	8 (16.6%) 1.5 (0.7-3.1)	781 (11.3%) Ref	1.0 (0.5-2.6)	0.7 (0.4-1.4)	1.5 (0.7-3.4)
Longer than 6 months n (%) OR (95% CI)	23 (25.8%) 1.0 (0.6-1.6)	21 (18.1%) 0.6 (0.4-1.1)	19 (39.5%) 1.7* (0.9-3.1)	1,730 (25%) Ref	0.9 (0.5-1.5)	0.6 (0.4-1.1)	1.9* (1.0-3.5)

*$p \leq .05$, ** $p < .001$ vs. general population ($n = 6,883$). Odds Ratios (OR) with 95% Confidence Intervals (CI) [2]Adjusted for maternal age at delivery, parity, maternal educational level and pre-pregnancy smoking and partner's age.

This table is reproduced from: Easter, A., Treasure, J. and Micali, N. (2011), Fertility and prenatal attitudes towards pregnancy in women with eating disorders: results from the Avon Longitudinal Study of Parents and Children. BJOG: An International Journal of Obstetrics & Gynaecology, 118: 1491–1498. doi: 10.1111/j.1471-0528.2011.03077.x

Study 2: Longitudinal dietary patterns in children of women with lifetime eating disorders

Results from full models are reported in Easter et al. (328).

'Snack' dietary pattern

Consumption of 'snacks' at 3 years was found to be similar in the children of women in the three ED groups compared to the unexposed children. After adjusting for confounding variables there were no differences between children in the maternal ED groups and the unexposed group (AN: adjusted coefficient = −0.461, [−0.227, 0.135]; BN: adjusted coefficient = −0.007, [−0.145, 0.159]; and AN+BN: adjusted coefficient = 0.903, [−0.139, 0.320].

'Health conscious' dietary pattern

Children of mothers in all three ED groups had higher scores on the 'health conscious' dietary pattern across the four time-points, compared to children in the unexposed group. After adjusting for covariates, these differences persisted in the maternal AN and maternal BN groups (AN: adjusted coefficient = 0.355, [0.162, 0.547]; BN: adjusted coefficient = 0.209, 0.044, 0.373]; and AN+BN: adjusted coefficient = 0.131, [-0.131, 0.395].

Male children of women in the AN group were less likely to adhere to this pattern than females; conversely male children of mothers reporting both AN+BN were more likely to have higher scores on the health conscious pattern compared to female children (full models available in (328)).

'Traditional' dietary pattern

Children in all exposed groups scored lower on the 'traditional' dietary pattern across the four time-points, compared to children in the unexposed group. After adjusting for covariates these differences persisted in the maternal AN and maternal BN groups, and a trend remained in the maternal AN+BN, compared to the unexposed group. (AN: adjusted coefficient = -0.241, [-0.463, -0.018]; BN: adjusted coefficient = -0.372, [-0.560, -0.184]; and AN+BN: adjusted coefficient = -0.279, -0.592, 0.032].

'Processed' dietary pattern

Scores on the 'processed' dietary pattern were similar in the maternal ED groups, compared to children in the unexposed group, in both adjusted and unadjusted models. Full models can be found in Easter et al. (328).

Study 3: Growth trajectories in children of women with lifetime eating disorders

Male children

Boys of women with AN+BN had higher predicted heights than male children of women with no ED between birth and 5 years of age, and birth and 10 years of age, see Table 31. This remained after adjusting for potential confounders. For boys of women with BN the group difference in predicted heights became larger with age, reaching 1.88 cm taller by age 10 (see Table 31). On the other hand, the difference for boys of women with AN was the opposite, and by age 10, they were 0.75 cm shorter than unexposed women.

Both children of women who reported AN+BN as well as children of mothers with other psychiatric disorders were shorter from birth until 10 years old. Specifically, we found that the biggest difference in height was in children of mothers with other psychiatric disorders.

Female children

Girls of women with AN and AN+BN, (between birth and 5 years of age, birth and 10 years of age respectively), had lower predicted heights than girls in the unexposed group (see Table 32). After adjusting for covariates, girls of women with AN height's was were expected to be shorter than girls in the unexposed group by 0.47cm.

On the other hand, early in childhood, girls of women with BN height's were expected to be similar to girls of mothers in the unexposed group. At the age of 5, girls of women with BN were slightly shorter and from 5 to 10 years of age the differences in predicted height were larger, reaching 0.64 cm shorter than children of mothers in the unexposed group (see Table 32).

Children of women with other psychiatric disorders had a tendency to be shorter during childhood; however, when compared to girls of women with AN and AN+BN, these differences were comparably smaller for this group, see Table 32.

Table 31: Mean predicted anthropometry for boys across categories of maternal eating disorder, with adjustment for standard confounders (gestational age, maternal age, maternal education, parity).

	Mean predicted anthropometry (*SD*) of offspring of unexposed women	Mean difference (*SD*) from unexposed for offspring of women with:			
		AN	BN	AN+BN	Other psychiatric disorders
Height (cm)	*n* = 4588	*n* = 74	*n* = 85	*n* = 38	*n* = 501
Birth	50.3 (5.4)	+0.14 (2.0)	+0.17 (2.08)	-0.10 (2.0)	-0.20 (2.2)*
1 year	76.1 (5.4)	+0.32 (2.4)	+0.05 (2.4)	-0.09 (2.4)	-0.28 (2.5)**
2 years	87.3 (5.4)	+0.40 (3.0)	+0.01 (3.1)	-0.10 (3.0)	-0.32 (3.2)*
5 years	110.2 (6.8)	+0.39 (4.5)	+0.15 (4.5)	-0.17 (4.4)	-0.42 (4.7)*
10 years	140.7 (8.8)	-0.75 (7.3)	+1.88 (7.5)**	-0.81 (7.1)	-0.64 (7.9)$
PI (kg/m^3)	*n* = 4537	*n* = 73	*n* = 84	*n* = 38	*n* = 496
Birth	26.1 (5.4)	-0.43 (2.5)	-0.28 (2.6)	+0.07 (2.5)	+0.13 (2.7)
1 year	23.3 (4.7)	-0.12 (2.1)	+0.41 (2.2)$	+0.27 (2.1)	+0.22 (2.3) *
BMI (kg/m^2)	*n* = 4271	*n* = 68	*n* = 78 8.31	*n* = 35	*n* = 452
2 years	16.8 (3.9)	+0.10 (2.0)	+0.26 (1.9)	+0.32 (1.7)	+0.15 (2.0)$
5 years	15.9 (3.9)	+0.34 (1.4)*	+0.12 (1.3)	+0.49 (1.4)*	-0.02 (1.5)
10 years	17.7 (4.6)	+0.09 (3.3)	+0.12 (3.2)	+0.08 (3.2)	+0.09 (3.6)

a Values are predicted from the multilevel models, and represent the predicted anthropometry for offspring of mean gestational age (39.4 weeks) and with a mother with the following characteristics: mean age (28.2 years), less than O-level education, parity of zero. P values are from Z-tests comparing each group to the offspring of women with no eating or other psychiatric disorder. $: p ≤ 0.1 *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

This table is reproduced from: Easter, A., Howe, L. D., Tilling, K., Schmidt, U., Treasure, J., & Micali, N. (2014). Growth trajectories in the children of mothers with eating disorders: a longitudinal study. BMJ Open, 4(3), e004453.

Table 32: Mean predicted anthropometry for girls across categories of maternal eating disorder, with adjustment for standard confounders (gestational age, maternal age, maternal education, parity).

	Mean predicted anthropometry (*SD*) of offspring of unexposed women	Mean difference (*SD*) from unexposed for offspring of women with:			
		AN	BN	AN+BN	Other psychiatric disorders
Height (cm)	*n* = 4416	*n* = 65	*n* = 82	*n* = 30	*n* = 432
Birth	49.7 (5.3)	-0.47 (1.9)$^\$$	-0.08 (2.1)	+0.23 (2.0)	-0.16 (2.2)$^\$$
1 year	74.3 (5.3)	-0.27 (2.4)	+0.05 (2.4)	-0.73 (2.4)$^\$$	-0.18 (2.6)$^\$$
2 years	85.6 (5.3)	-0.24 (3.0)*	+0.02 (3.0)	-0.93 (3.0)$^\$$	-0.18 (3.2)
5 years	109.6 (6.0)	-0.31 (4.3)	-0.18 (4.3)	-0.94 (4.2)	-0.17 (4.8)
10 years	138.9 (8.6)	-0.57 (7.0)	-0.65 (6.9)	-0.32 (6.7)	-0.12 (7.5)
PI (kg/m3)	*n* = 4363	*n* = 64	*n* = 81	*n* = 30	*n* = 424
Birth	26.2 (5.3)	-0.07 (1.9)	+0.48 (2.2)*	-0.16 (2.2)	-0.09 (2.3)
1 year	23.2 (5.3)	+0.39 (2.4)$^\$$	+0.06 (2.5)	+0.39 (2.7)	-0.22 (2.7)$^\$$
BMI (kg/m2)	*n* = 4117	*n* = 61	*n* = 78	*n* = 29	*n* = 398
2 years	16.6 (3.9)	-0.35 (1.9)$^\$$	+0.30 (1.9)	+0.25 (1.8)	-0.07 (2.1)
5 years	16.0 (3.9)	-0.01 (1.5)	+0.26 (1.5)$^\$$	+0.32 (1.5)	+0.16 (2.1)*
10 years	18.1 (5.1)	+0.03 (3.5)	-0.29 (3.4)	-0.52 (3.3)	+0.56 (3.7)**

a Values are predicted from the multilevel models, and represent the predicted anthropometry for offspring of mean gestational age (39.4 weeks) and with a mother with the following characteristics: mean age (28.2 years), less than O-level education, parity of zero. P values are from Z-tests comparing each group to the offspring of women with no eating or other psychiatric disorder. $: $p \leq 0.1$ *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$

This table is reproduced from: Easter, A., Howe, L. D., Tilling, K., Schmidt, U., Treasure, J., & Micali, N. (2014). Growth trajectories in the children of mothers with eating disorders: a longitudinal study. BMJ Open, 4(3), e004453.

PI and BMI Differences across ED group

<u>Male children</u>

Figure 5 and Figure 6 show group differences in the trajectories of PI and BMI in boys. There was not statistical evidence of growth differences for all periods; in a large number of cases we found large standard deviations, this can be due to maternal ED groups being small.

After adjusting for covariates, the PI was lower for boys of women with AN compared to boys of unexposed women. Children of women across all exposed groups had higher BMI between the ages of 2 and 10 compared to those of unexposed women. At five years of age children's predicted BMI in the maternal AN group was 0.34 kg/m² higher than children of unexposed mothers. The BMI of boys of women with AN and AN+BN at 10 years of age was similar to those of boys of unexposed women (see *Table 38).* A tendency towards higher PI at 2 years was found in the boys of mothers with other psychiatric disorders, however, their BMI trajectories a few years later were similar to those of boys of mothers in the unexposed group.

<u>Female children</u>

Girls of women with BN had higher PI at birth compared to girls of unexposed women, however, this difference was reduced by the time they turned 12 months.

Girls of women with BN and AN+BN continued to have higher BMI than girls of unexposed mothers until the age of 5 (see Figure 6); however, their BMI was comparable to girls of unexposed women by the time they turned 10 years old. On the other hand, girls of women with AN had lower BMI than girls of unexposed women during early childhood; however, their BMI was comparable to girls of unexposed women years later (late childhood) (see Figure 6). The BMI changes through childhood of girls of women who reported other psychiatric disorders was comparable to children in the AN group (see Figure 6*)*; conversely, at the age of 10, their expected BMI was on average 0.56 points higher than girls of unexposed mothers.
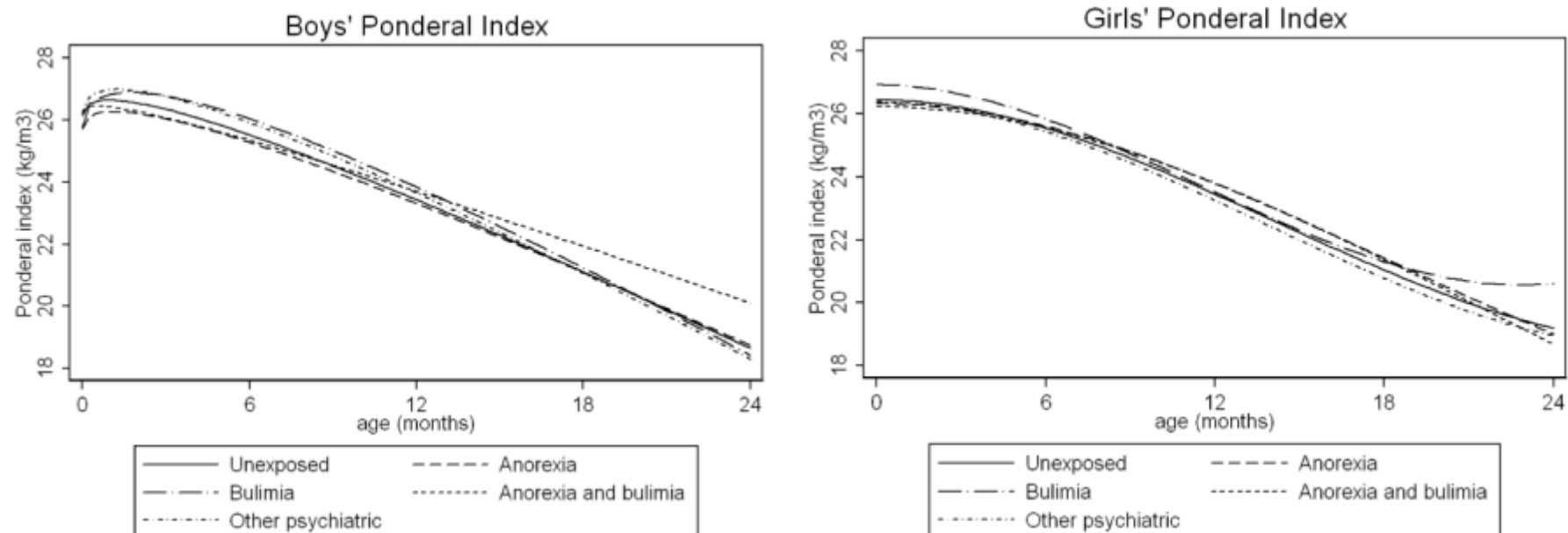
Figure 5: Average fractional polynomial curve of ponderal index trajectories for girls and boys by maternal eating disorder, birth to two years, adjusted for confounders

Note: Values are predicted from the multilevel models, and represent the predicted anthropometry for offspring of mean gestational age (39.4 weeks) and with a mother with the following characteristics: mean age (28.2 years), less than O-level education, parity of zero

This figure is reproduced from: Easter, A., Howe, L. D., Tilling, K., Schmidt, U., Treasure, J., & Micali, N. (2014). Growth trajectories in the children of mothers with eating disorders: a longitudinal study. BMJ Open, 4(3), e004453.
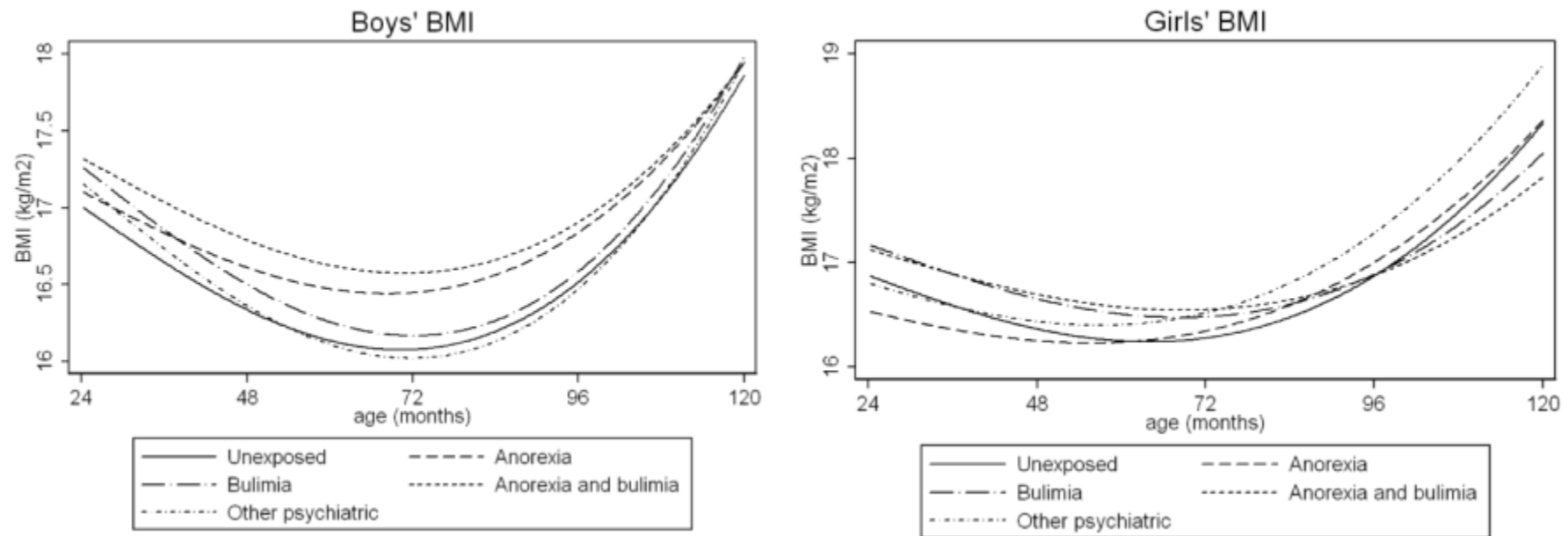
Figure 6: Average fractional polynomial curve of BMI trajectories for girls and boys by maternal eating disorder, two to ten years, adjusted for confounders

Note: Values are predicted from the multilevel models, and represent the predicted anthropometry for offspring of mean gestational age (39.4 weeks) and with a mother with the following characteristics: mean age (28.2 years), less than O-level education, parity of zero

This figure is reproduced from: Easter, A., Howe, L. D., Tilling, K., Schmidt, U., Treasure, J., & Micali, N. (2014). Growth trajectories in the children of mothers with eating disorders: a longitudinal study. BMJ open, 4(3), e004453.

Discussion

The overall aim of the studies was to investigate the effects of maternal ED on fertility and on their children's dietary patterns and growth trajectories.

ED and fertility

Study one highlighted that women with ED experience more difficulties conceiving. Results showed that women with a lifetime diagnosis of AN (both AN and AN+BN) had a higher chance of visiting a doctor for problems conceiving compared to unexposed women. Although only a small percentage of women actually received treatment during the time trying to conceive in this sample, we found that women with AN and BN were twice as likely to undergo treatment for problems with conception. Based on these results, it could hypothesise that problems with fertility in this sample may be secondary to low BMI, which is present in both groups.

Results showed that women who reported both AN and BN has higher odds of taking longer than 6 months to conceive compared to unexposed women. Importantly, this group, had the lowest BMI before conception and higher prevalence of lifetime purging when compared to the other two groups (317). The severity in this group may lead to a higher risk for both fertility problems and delays in conceiving.

Approximately 40% of women in the sample who reported having AN, reported that their pregnancy was unintentional. Research has shown that ovulation and pregnancy can still occur in women with ED who have irregular cycles ((329). Therefore, the large percentage of unintentional pregnancies found in this sample, may be due to erroneous beliefs about their ability to become pregnant.

Diet and growth in children of women with eating disorders

Study two and three explored potential differences in diet and growth between the ages of three and nine, and growth trajectories between birth and ten in children of women with ED.

Children of mothers with ED were found to be less likely to adhere to a 'traditional' dietary pattern, than children of women without ED. This pattern is synonymous with a British 'meat and two veg diet', which would typically be eaten at mealtimes. Family mealtimes are particularly difficult for mothers who have experienced an ED (330) and they have been found to be less likely to regularly cook or eat with their children (331). Reduced adherence

to the 'traditional' dietary pattern in this study may reflect less frequent mealtimes in families where the mother has an ED.

In line with suggestions from previous research that children of women with ED may consume less junk foods (315), children of mothers reporting either AN or BN showed to stay on a more 'health conscious' diet. We have previously shown that women with AN in this sample were more likely to follow this dietary pattern in pregnancy themselves (332); these findings might imply a stronger maternal desire for women with ED to provide a healthy diet for their children.

It is currently not know what effects increased exposure to a health conscious/vegetarian diet during childhood may have on long-term development and health of children of women with ED, previous evidence form this sample suggests associations with positive developmental outcomes (333, 334).

Changes across childhood

Over time children of women with ED were adhering to a more 'traditional' and less 'health conscious' dietary pattern. These findings may reflect the influence of other societal effects on diet, such as school, and consequentially children in the exposed groups having greater influence over their diet. Alternatively, these findings may reflect differences in maternal feeding styles in early childhood. It has previously been reported that mothers with ED display more restrictive feeding styles (300, 335); however, studies suggested that parental restricting high fat and palatable foods may in fact increase their desirability (336-338).

Gender differences

Some previous studies have indicated that maternal transmission of weight concerns and dieting behaviours may be stronger for girls than boys (339, 340). In the present investigation, female children of mothers with AN were more likely to adhere to the "health conscious" pattern than males, suggesting a stronger maternal influence on girls of women with AN.

Past investigations have proposed that the offspring of women with BN may be at risk of having problems with obesity (314, 341); findings from the present study showed that boys of women from all exposed groups had higher adiposity than boys of unexposed women, with the difference being more pronounce at the age of five. Taking into consideration that boys of mothers with other psychiatric problems have similar BMI trajectories to those of unexposed

mothers, the differences we found in growth trajectories in the offspring of mothers with ED may be specific to maternal eating pathology. One possible hypothesis is that a fast increase in growth during earlier years may put them at higher risk for obesity later in life as well as other health problems.

BMI trajectories in female children of women with ED were different to those of boys and show a fluctuating pattern throughout childhood. Specifically, girls of women with BN and AN+BN had a tendency for higher BMI in early years but lower BMI at 10 years old. On the other hand, girls of women with AN had a higher BMI in earlier years and a more similar BMI to healthy controls by the age of 10. We are not clear on the consequences of the growth trajectories at long-term. However, a recent study found that growth patterns were predictive of later AN (342). A possibility is that differences in growth trajectories in children of mother with AN highlighted by this study are in some way related to dietary patterns during childhood, however, we were not able to investigate this association.

Compared to boys of unexposed women, boys of women with BN from the age of two onwards, were found to be taller. On the other hand, compared to boys of unexposed women, boys of women with AN were only taller during early childhood, and were found to be shorter by the time they reached 10 years old. Girls of women with ED, predominantly AN, had a tendency to be shorter than unexposed children. These findings may show that this group is at specific risk of having a more restricted growth during childhood. Furthermore, these results are similar to previous case studies and those with younger children, that show that children of women with AN do not grow as much as those of unexposed women (320, 341, 343).

Past research has shown that mothers with ED are more concerned with their daughter's weight and shape compared to their sons (344), who may have a higher chance of becoming underweight (341). Results from the current studies support gender specific growth trajectories; however, as our growth models were built separately for both genders, were unable to could not examine gender interactions.

Conclusions

In conclusion, the investigations undertaken in this chapter highlight novel findings regarding the effects of maternal ED on fertility and their children's development. Women with ED were found to experience difficulties in the pre-conception period and in post-natal

differences in the dietary patterns and growth trajectories of children born to women with ED were highlighted.

Our study is the first to investigate longitudinal growth and diet patterns in children of women with lifetime ED and therefore, needs replication and additional examination of the pathways. Nonetheless, health professionals need to be conscious of the associations between maternal ED and their children's growth so that they can better guide both the mother's health and the development of the foetus. Continuity of care for this group of women is paramount from before conception into the post-natal period. Furthermore, and at a public health level, it is of extreme importance to further analyse underlying mechanisms of growth differences in children of women with ED. Following on from this study we are now developing an intervention for pregnant women with ED, aimed at preventing adverse child outcomes.

Chapter 10. Specialist and non-specialist care pathways for adolescents with anorexia nervosa (WP7a)

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An abbreviated version of this chapter has been published the International Journal of Eating
Disorders (345).

Abstract

Word count: 180

Background: There is now a significant body of research demonstrating the efficacy of specific treatments for adolescent anorexia nervosa, little is known about the way in which different service contexts impact treatment outcome. The present study investigates the role of specialist outpatient services and how the availability of such services influences the rates of referrals, hospital admissions, continuity of care and service user experiences.

Methods: Mental health services in London were asked to identify adolescents who presented for treatment for eating disorder over a two-year period. Retrospective data about service use, including the need for hospital admissions, was collected from clinical casenotes. A small sample of adolescents and parents were interviewed about their experiences of services.

Results: Direct access to specialist outpatient services was associated with higher referral rates, lower admission rates, and greater consistency of care. Service users identified a number of advantages of specialist service provision.

Conclusions: Data from the present study suggest that facilitating direct access to specialist services for adolescents with anorexia nervosa may result in better outcomes, lower costs, and higher satisfaction among service users.

Introduction

The rapid physical and psychological deterioration that can occur in young people with anorexia nervosa (AN) means that early intervention with the potential for intensification of care is important. Clinical trials suggest that outpatient family-based treatments are effective in the short- and longer-term (282, 346-348). However, treatment in inpatient settings is relatively common. Data from the UK suggest admission rates for children and adolescents of 35-50% (30, 349) and, in one survey, young people with eating disorders occupied more child and adolescent psychiatric beds than any other diagnostic group (31). Studies of inpatient care have found no evidence of specific benefits arising out of hospital treatment in comparison with outpatient care (350), and there is some evidence that prolonged admissions may have worsen outcome (351), as well as being more costly (352).

There is considerable variability in the treatment provisions for children and adolescent suffering from AN in the UK ranging from outpatient treatment provided within general child and adolescent mental health services (CAMHS) to highly specialised eating disorders services. The only randomised controlled trial to compare general and specialist outpatient services, the Treatment Outcome for Child and adolescent Anorexia Nervosa (TOuCAN) trial, found no difference in clinical outcomes between services (353). Prior to the present study, outcomes following treatment as usual in general and specialist outpatient services had not been compared, so to date it has been difficult to separate the effects of specific treatments from the effect of service specialisation.

The present study provides a naturalistic comparison of alternative service provisions for adolescent AN in the UK, using Greater London with a population of approximately 7.8 million – as an exemplar. We hypothesised that we would find two main care pathways, shaped by the availability of different outpatient services in the form of general CAMHS services or specialist child and adolescent eating disorders services. We aimed to explore associations between these different care pathways and [1] the number of cases seen in services beyond primary care, and [2] rates of admission for inpatient treatment (excluding admission for acute medical stabilisation only). We also aimed to explore the experiences of adolescent service users and their parents.

Methods

Study 1: Quantitative study

The design of the study was a naturalistic, retrospective cohort study, using clinical casenotes as the primary data source. Our main hypotheses were: [1] accounting for population size, more adolescents with AN and restricting eating disorders not otherwise specified (EDNOS-AN) from the specialist care pathway than from the general care pathway would present to services beyond primary care; and [2] controlling for severity of presentation, a lower proportion of adolescents with anorexia nervosa and EDNOS-AN from the specialist care pathway than from the general care pathway would be admitted for inpatient treatment during the first year of treatment.

Service mapping, recruitment and categorisation

An initial phase was to identify existing services for adolescents with eating disorders in London. This included searches of the websites of public and private healthcare providers, the UK Government-funded children's service mapping exercise (2007-8) and publications by the Royal College of Psychiatrists (26, 354). The identified services were asked to confirm arrangements for managing eating disorders in their area and return a questionnaire about the treatments their service provided. This information was used to compile a list of eligible services that where then was asked to participate in the study.

Outpatient services were categorised either as general CAMHS or specialist eating disorders services drawing on existing criteria (26, 355) to define specialist outpatient eating disorders services: a minimum of 25 new eating disorders referrals per year; a multi-disciplinary team, including medical and non-medical staff and more than one person with experience of treating eating disorders; a team with the expertise to deliver evidence-based treatments, and the resources to offer routine outpatient treatment. Inpatient services were categorised into specialist eating disorders units and general psychiatric units.

Case identification

Each service was asked to identify individuals that met the following criteria:

1. Having initial face-to-face contact with the service, or re-contact after a treatment break of at least six months, between 1 December 2006 and 30 November 2008

2. Age 13-17 years at the time of initial contact (or re-contact)

3. A primary diagnosis of an eating disorder

4. Being registered with a GP from a London Primary Care Trust (PCT; the commissioning bodies at the time, which determined service accessibility).

In each service potential participants were identified through searches of electronic patient records, correspondence with service users, clinical diaries, referral lists, funding records or audit data.

Participant recruitment and participant-level data collection

Potential participants were contacted by post, asking for permission for us to access their clinical casenotes. A standard item sheet was used to record data for each participant, including their PCT, demographic data such as age and sex, details of symptoms, and use of treatment and services in the 12 months after entry in to the service. Limited, anonymised data (as agreed with Ethics) was collected from services about non-consenters to avoid inclusion of duplicates and enable comparisons between consenters and non-consenters.

Data analysis

To evaluate the number of cases seen beyond primary care (Hypothesis 1), pathways were defined reflecting the agreements between PCTs and services defining the type of outpatient service that was typically made available following referral from primary care. The care pathway for each adolescent was therefore defined by the typical funding arrangements of the PCT in the relevant catchment area. For this analysis data for both consenters and non-consenters were included.

'Presentation rates' were calculated for each PCT, using the number of cases identified by services and population statistics from the Office for National Statistics (pop.info@ons.gsi.gov.uk). Separate calculations for females and males were done for each PCT using the following formula:

Presentation rate of N cases per 100,000 population of 13-17 year-olds per year = [N cases identified / (population of 13-17 year-olds in 2007+2008)] x 100,000.

Mean presentation rates were compared between PCT groups by ANOVA using diagnostic plots to check that required assumptions held. In particular, when PCT groups were compared

we carried out two planned comparisons – of CAMHS PCT groups against the specialist service PCT group.

To evaluate differences in admission rates (Hypothesis 2) only data from consenting participants could be used. To assess the representativeness of the sample, comparisons of personal, symptomatic and service variables were made between 'consenters' and 'non-consenters'. Independent samples t-tests were used to compare groups on continuous variables. Chi-squared tests or Fisher's Exact Tests were used to compare groups on categorical variables. Care pathway groups were established in two ways: by PCT, as for Hypothesis 1, and by the actual care pathway that each participant followed. Binary logistic regression was used to compare rates of admission for inpatient treatment between the groups controlling for the severity of presentation (measured by degree of underweight).

Power calculation

A power calculation was performed, based on the expectation of two main care pathways (starting with either a specialist outpatient eating disorders service or a general CAMHS) and estimated admission rates of 10% (from audit data) and 35%, respectively. A chi-squared test at a significance level of 5% to detect a difference with a power of 80% indicated that 43 participants per group would be needed to show a statistical difference.

Ethical approval

The study was reviewed by the Royal Free Hospital and Medical School REC (ref. 07/H0720/119). We were concerned that obtaining consent from participants would affect the extent to which general CAMHS were represented. We anticipated that they would have fewer eligible patients and fewer resources to dedicate to recruitment than specialist services, which could result in both a small total number of participants and a lower proportion of those who were suitable being recruited from general services than from specialist services. The Patient Information Advisory Group (PIAG) was approached for permission to access case notes without obtaining consent but the application was not approved. Subsequently, the National Information Governance Board, which replaced PIAG, gave permission to store non-consenters' initials and dates of birth, enabling removal of duplicates from the non-consenting sample (ref. ECC 6-06(I)/209).

Study 2: Qualitative study

For the qualitative part of the study, a sub-sample of adolescents was selected from those who allowed us to access their casenotes for the quantitative study. The main aim of sampling was to select people with experience of the different care pathways. Fifty-six adolescents were asked whether they would be willing to take part in an interview about their experiences of treatment and services, and were also asked for permission to contact their parents about taking part in a similar interview. Interviews were based on an interview guide, rather than a fixed interview schedule. The focus was on the participant's journey through services and experience of each stage of treatment. Questions were non-directive and open-ended. Interviews were transcribed verbatim and analysed using thematic analysis.

Results

Study 1: Quantitative study

Service mapping, recruitment and categorisation

Forty-four eligible services were identified, of which 37 provided the required data. Table 33 shows the services by category. Service mapping and recruitment revealed a potentially substantive difference between general CAMHS: some defined themselves as non-specialist in eating disorders, while others described having a specialist eating disorders 'mini-team' within the general team. CAMH services were therefore categorised into self-defined 'specialist ED CAMHS' and 'non-specialist CAMHS'. To take this into account the original plan of statistical analysis was modified to include pairwise comparisons between care pathways based on specialist eating disorders services and care pathways based on both types of CAMHS.

Table 33: Services by category

	Participating services	Non-participating services
NHS outpatient services		
Specialist child and adolescent eating disorders services	2	0
Other eating disorders services	3 (1 child, 2 adult*)	0
Specialist CAMHS	7	2
Non-specialist CAMHS	15	2
NHS inpatient services		
Specialist eating disorders units	4 (1 child & adolescent, 3 adult*)	0
General psychiatric units	2	1
Private services		
Specialist eating disorders units	6 (4 child & adolescent, 2 adult)	2 (1 child & adolescent, 1 adult)

*Two of these are the same service (i.e. two adult services provided both outpatient and inpatient care)

Presentation rates to services beyond primary care

PCT groups

Three PCT groups were identified, based on the care pathway they typically commissioned to provide outpatient treatment following referral from primary care: (1) a specialist child and adolescent eating disorders service (CAEDS), (2) a specialist CAMHS and (3) a non-specialist CAMHS. In the CAEDS group, some PCTs allowed referrals to bypass CAMHS completely, some required CAMHS to authorise referrals, and others required CAMHS to assess adolescents before referring them for treatment in an eating disorders service. In the specialist and non-specialist CAMHS groups, assessment and treatment were provided by the same service. Specialist CAMHS differed from CAEDS in that they each served a single PCT, while CAEDS each served a number of PCTs. All PCTs had access to general paediatric medical units. Depending on the area, longer-term inpatient treatment was provided by public or private eating disorders units or general adolescent psychiatric units.

Services identified 641 potentially suitable cases. Using initials, dates of birth and PCTs, duplicates were identified and removed, leaving 489 cases. After checking eligibility for the study, 111 cases were excluded. The final number of cases meeting inclusion criteria was 378. Services from four PCTs did not provide any data and were excluded from the analyses. Therefore, a total of 27 PCTs and 367 cases were included in the subsequent analyses. The grouping of these is shown in Table 34.

Table 34: Identified cases by PCT group

PCT group	AN and EDNOS-AN		BN and EDNOS-BN		ED*		Total
	Female	Male	Female	Male	Female	Male	
Child and adolescent eating disorders services (12 PCTs)	112	8	62	1	25	1	209
Specialist CAMHS (5 PCTs)	50	3	15	0	5	0	73
Non-specialist CAMHS (10 PCTs)	38	3	10	3	28	3	85
Total	200	14	87	4	58	4	367

*Cases where services did not provide a more detailed diagnosis than 'eating disorder'

The total number of males in the overall sample was small ($n = 22$) making it inappropriate to include them in the analyses. Data from the services could be used to provide a clear diagnosis for 287 females. Of these, 200 were AN or EDNOS-AN and 87 were BN or EDNOS-BN. For part of the sample (58 females), however, the services only gave a diagnosis of 'eating disorder' and there was insufficient data for a researcher to place these individuals into one of the specific diagnostic groups. Presentation rates were therefore calculated in two ways. First using cases with a known diagnosis, to give an 'observed presentation rate', and second based on the assumption that the same proportion of missing and known cases were AN or EDNOS-AN (69.7%) and BN or EDNOS-BN (30.3%) to give an 'estimated presentation rate'. As the focus of this study is restricting eating disorders, only results for this subgroup are presented.

Figure 7 shows the presentation rates of AN and EDNOS-AN by PCT group. Unadjusted pairwise comparisons show that the presentation rates for the non-specialist CAMHS group were significantly lower than those of the specialist eating disorders service group (observed rate: $p < 0.01$; estimated rate: $p = 0.04$). The presentation rates of the specialist CAMHS group did not differ significantly from those of the CAEDS group (observed rate: $p = 0.41$; estimated rate: $p = 0.98$).
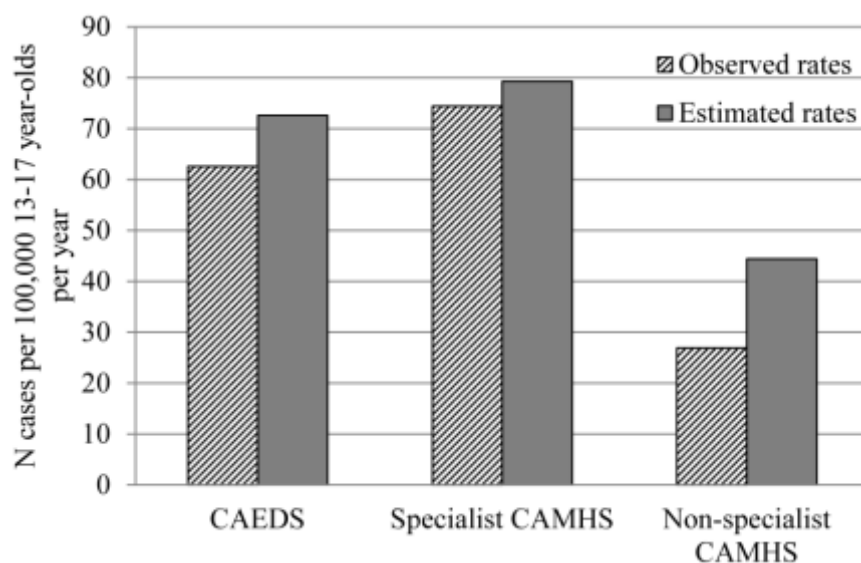
Figure 7: Observed and estimated presentation rates of anorexia nervosa and EDNOS-AN by PCT group

Comparison of participant characteristics of consenters and non-consenters

Of the 378 adolescents meeting entry criteria, 127 (33.6%) gave consent for a researcher to access their clinical case notes, 15 (4.0%) actively refused consent, 235 (62.2%) did not respond, and 1 (0.3%) had died, having withdrawn from treatment in a non-specialist CAMHS. The distribution of diagnoses (AN, EDNOS-AN, BN and EDNOS-BN) did not differ between the consenters and the non-consenters ($p = 0.16$). Subsequent comparisons include only the 220 adolescents with AN or EDNOS-AN (the 214 cases shown in Table 34, plus six cases from the PCTs that were excluded from the analyses of presentation rates), 93 (42.3%) of whom consented to participate in the study.

No statistically significant differences were found between consenters and non-consenters in mean age at assessment, sex, ethnicity, proportion with a diagnosis of AN (vs EDNOS-AN),

mean body mass index at assessment, proportion who were binge-eating or self-induced vomiting, first service attended following referral from primary care, or proportion admitted as inpatients during the study period. A higher proportion of consenters (47.3%) than non-consenters (31.8%) accessed more than one participating service during the study period, but this difference did not reach statistical significance ($p = 0.06$). The only significant difference identified between consenters and non-consenters was the PCT group to which they belonged. A significantly higher proportion of those belonging to the CAEDS service group (55.0%) consented to be part of the study than those who belonged to the specialist CAMHS group (26.3%; $p < 0.01$) and the non-specialist CAMHS group (23.3%; $p < 0.01$).

Characteristics of the consenting sample are shown in Table 35. The average weight   is higher than would be expected from a sample of adolescents with anorexia nervosa, due to the inclusion of EDNOS-AN. Average weight loss prior to assessment was 12.3kg, which is substantial considering the relatively short mean duration of illness (8 months). There were low rates of binge eating, self-induced vomiting and laxative misuse. No statistically differences were found between the groups in mean age at assessment, sex, ethnic background, percent median BMI at assessment, proportion who were binge eating, vomiting or source of referral.

Table 35: Characteristics of the consenting sample at assessment

Mean age	15.1 years ($SD = 1.2$)
Sex	90 (96.8%) female, 3 (3.2%) male
Ethnicity	64 (68.8%) White British, 23 (24.7%) other, 6 (6.5%) missing
Social class	62 (66.6%) I/II, 10 (10.8%) IIIN/IIIM, 3 (3.3%) IV/V, 18 (19.4%) missing
Parents' relationship status	70 (75.3%) intact, 18 (19.4%) separated, 3 (3.3%) other, 2 (2.2%) missing
Diagnosis	57 (62.6%) anorexia nervosa, 34 (36.6%) EDNOS-AN, 2 (2.2% missing)
Mean weight for height %	82.8 ($SD = 10.4$, range = 63.3–131.9)
Menstrual status (females)	55 (61.8%) amenorrhoea, 18 (20.2%) irregular periods, 6 (6.7%) regular periods, 2 (2.2%) on hormonal contraceptives, 8 (9.0%) missing
Mean duration of illness	8.1 months ($SD = 8.0$, range = 1–36)
Binge eating	81 (87.1%) no, 9 (9.7%) yes, 3 (3.2%) missing
Self-induced vomiting	69 (74.2%) no, 21 (22.6%) yes, 3 (3.2%) missing
Laxative misuse	82 (88.2%) no, 27 (7.5%) yes, 4 (4.3%) missing
Exercise for weight loss	44 (47.3%) no, 43 (46.2%) yes, 6 (6.5%) missing
Primary care referrer	65 (69.9%) GP, 9 (9.7%) school/college, 6 (6.5%) paediatric inpatient unit, 3 (3.2%) hospital outpatient dept., 5 (5.4%) CAMHS (seen for other issues), 1 (1.1%) counselling service, 1 (1.1%) parent, 3 (3.2%) missing

Expected and actual care pathways

It became clear during the early part of the study that the PCT agreements did not always predict the actual care pathway that individual patients followed. When the actual care pathways were examined, the data suggested a greater similarity than expected between specialist CAEDS and specialist CAMHS (in terms of the number of cases presenting for treatment and the proportion admissions for inpatient treatment within 12 months). Therefore, these services were grouped for subsequent analyses, and the following 'actual care pathway groups' were formed:

(1) Specialist assessment to specialist treatment: participants referred directly from primary care to a specialist CAEDS (child and adolescent, or adult) or a specialist CAMHS for assessment and treatment

(2) Non-specialist assessment to specialist treatment: participants assessed in a non-specialist CAMHS and then immediately referred on to a specialist CAEDS for treatment

(3) Non-specialist assessment to non-specialist treatment: participants referred from primary care to a non-specialist CAMHS for assessment as well as treatment

Private assessment to private treatment: participants who moved from primary care into private eating disorder services (these were excluded from subsequent analyses, as the aim of the present study was to explore care pathways within the NHS). Table 36 compares the actual care pathways with those that would be predicted by PCT agreements. The main difference was that some of the CAMHS services that were in the catchment area of one of the CAED services did not automatically refer on following an assessment and more people than expected were assessed and started treatment in generic CAMHS.

Table 36: Actual versus expected care pathways

Care pathway	Expected pathway (based on PCT)	Actual pathway
Specialist assessment to specialist treatment	71	53
Non-specialist assessment to specialist treatment	10	16
Non-specialist assessment to non-specialist treatment	9	15
Private assessment to private treatment	0	6

Admissions for inpatient treatment by actual care pathway

In the specialist assessment to specialist treatment group, 8/53 adolescents (15.1%) were admitted to hospital, compared with 3/16 (18.8%) in the non-specialist assessment to specialist treatment group and 6/15 (40.0%) in the non-specialist assessment to non-specialist treatment group. The binary logistic regression analysis (controlling for baseline percentage median BMI) indicated that the chance of admission in the non-specialist assessment to specialist treatment group was 32% higher than in the specialist assessment to specialist treatment group (adjusted $OR = 1.32$, 95% CI 0.30–5.81, $p = 0.71$), and the chance of admission in the non-specialist assessment to non-specialist treatment group was 261% higher than in the specialist assessment to specialist treatment group (adjusted $OR = 3.61$, 95% CI 1.00– 13.02, $p = 0.049$).

Continuity of care

The exploration of the actual care pathways identified an unexpected difference in continuity of care, depending on where outpatient treatment started. In the specialist assessment to specialist treatment group, 83% of participants completed their treatment in the same service, compared with 75% in the non-specialist assessment to specialist treatment group, and 41.7% in the non-specialist assessment to non-specialist treatment group. A post hoc analysis showed that the continuity of care was significantly higher in the specialist assessment to specialist treatment group than in the non-specialist assessment to non-specialist treatment group ($\chi^2 = 6.93$ $p < 0.01$).

Study 2: Qualitative study

Participant recruitment and characteristics

Eight adolescents and 11 parents agreed to take part in interviews about their experiences. As with the quantitative study, recruitment was more successful among those who had been to a specialist service. Of the adolescents, five had started treatment in a CAED service, two in a specialist CAMHS, and one in a generic CAMHS. The group of parents included one parent of each of the adolescents who took part in interviews, and three parents whose daughters did not want to participate: one of whom started treatment in a CAEDS, one in a specialist CAMHS, and one was assessed in a non-specialist CAMHS and then referred for treatment in CAEDS.

The nature of the sample means that the views reported here are not presented as being representative of any group other than that which took part in the interviews – however, they

provide an insight into the experiences of these families, and highlight factors that may impact on service user satisfaction. Full details of the studies and results are available elsewhere (356), and only a small number of quotes are presented here to demonstrate particular points.

Experiences of services

In nearly all cases of those we interviewed, help-seeking was prompted by a parent, rather than by the adolescent themselves, with some adolescents describing great resistance to the idea of external intervention.

> *"I don't really know what I thought was going on, I think I just thought I was losing a bit of weight and everyone was making a massive fuss and I was absolutely fine and please don't bother me because I'm quite happy just running my own show"*

While some general practitioners were supportive and facilitated access to treatment, others were viewed as decidedly unhelpful by adolescents and parents. Some GPs appeared to be guided more by physical signs, such as weight, than by parental concerns.

> *"The doctor said [to my parents] 'Oh no, your daughter's fine' ... that's when ... I was like 'Oh, I'm fine, I can just lose loads of weight"*

> *"The GP basically said that her BMI wasn't low enough to be anorexic ... she didn't mention a referral to CAMHS, she didn't mention [specialist service] ... if you got diagnosed with cancer, they would treat it, they wouldn't ... wait until you had Stage 3!"*

Adolescents who received treatment in CAMHS described situations where they felt they weren't receiving the help they needed, but were temporarily unable to access more specialist services.

> *"I wasn't getting any better ... I maintained a really frighteningly low weight for quite a long time ... I wanted to get better, I wanted some help ... I sort of said 'I've never had the opportunity to get better because I've never had proper help'"*

The parents of these adolescents expressed great relief when they were able to move to more specialist services, and regret that this hadn't happened immediately.

"CAMHS was like a holding bay"

"All three of us say 'If we hadn't have got to [specialist service], [daughter] would be dead'"

"Of course I feel sad when I think 'Well, what would our story have been if we'd come straight [to specialist service]?' ... I don't think she'd have been allowed to get [as ill as] she got last year"

Adolescents described the difficulty of moving between services and switching therapists, and explained that continuity with helpful relationships was valued.

"It's difficult to build that kind of relationship ... I felt like I was getting somewhere with [therapist] and then to start all over again with someone that didn't know me and didn't know the history ... it was quite frustrating because it's kind of like stopping and starting all the time and never really getting anywhere"

Clinicians' expertise in eating disorders was an important element of both adolescents' and parents' experiences of inpatient and outpatient services.

"A lot of it is expertise because I feel like 'ah, finally <u>someone</u> gets me' ... like, everything I say is something that [clinician] has already come across. She knows all of the symptoms so she doesn't make me feel like I'm a freak ... she just, she understands"

"You cannot compare [paediatric and specialist admission]. It's chalk and cheese. [The eating disorders unit] know what to look for, they know everything, you know, they know the natures of the beast"

For parents, one of the most unanimously positive experiences (for those who had taken part) was groups with other parents who were in a similar situation – these tended to be organised by specialist services. Those who didn't have access to groups were frustrated by this.

"It was a feeling that we were all ... there were all different types of people and different everything else, but we all had this problem"

"What I wanted was to talk to other people who were going through the same situation as me ... to meet up with somebody, to speak ... to see them face-to-face"

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Discussion

This is the first naturalistic study to examine outcomes following treatment as usual in different types of service for adolescents with an eating disorder. The key findings are: (a) once population size was taken into account, 2-3 times the number of adolescents with AN and EDNOS-AN were referred from primary care in areas with specialist outpatient services for child and adolescent eating disorders than in areas with no specialist services; (b) patients who started treatment in generic CAMHS were 2.5 times more likely to be treated in hospital during the following 12 months than those initially treated in a specialist service; and (c) continuity of care was considerably lower in non-specialist services, in that only 42% of adolescents started and continued treatment for the next 12 months without being referred on, compared to more than 80% of those seen in specialist services.

The number of cases seen in services beyond primary care

This is the most robust finding as it is based on the full sample of 367 cases. The low level of case identification in areas with no specialist services is consistent with previous research (26). The striking finding from this study is that the rate of referral to specialist services is close to the level that epidemiological studies suggest is the actual incidence of new cases seen in primary care (51, 357). It is possible that GPs with links to specialist services have better knowledge of eating disorders and their treatment and therefore identify and refer more cases than GPs with no specialist links. Alternatively, the visibility and easy access to specialist services may encourage referrals rather than a 'wait and see' approach that is sometimes seen in primary care. The second explanaton is supported by Currin's (358) primary care study, which showed that GP's working in areas where inpatient treatment was the only specialist service provision have higher referral thresholds than those in areas with specialist outpatient services. Our own clinical experience in a specialist context of receiving a growing number of very early referrals also supports this explanation. A third explanation is that availability of services has an effect on patient and/or parent preferences and changes the threshold for seeking help.

Admissions for inpatient treatment

While there have been previous clinical reports of reductions in admission rates following the development of specialist outpatient services (359), this is the first study that provides clear empirical support for this. Our study showed that admission for inpatient treatment was not predicted by service-level agreements between PCTs and service providers, but was predicted

by participants commencing treatment in a non-specialist CAMHS. The high level of admission in the non-specialist care pathway raises a number of concerns. Inpatient treatment of anorexia nervosa is costly (352, 360), has high relapse rates (226, 361), and there is evidence that hospital treatment is associated with poor outcomes in adolescent AN even when severity of symptoms are controlled for (351).

Continuity of care

In the present study, the differences in the continuity of care between the specialist care and non-specialist care pathway in was striking. This is important as continuity potentially reduces duplication of work, and avoids the need for managing transitions between services which can be problematic for patients and their families (36).

Service user experiences

Adolescent and parents highly valued the level of clinician expertise that they found in specialist services. Those who were dissatisfied with CAMHS were frustrated by barriers to specialist services. Movement between different services could disturb the delicate process of building and maintaining helpful therapeutic relationships and a lack of continuity of care could be experienced as being "sent from pillar to post" – this was one of the most frequent areas of dissatisfaction for those who were referred to CAMHS. Group interventions were particularly important for parents, and these are likely to be more easily facilitated by specialist services, due to the resources available and the greater number of families seen at any one time. Service user reports suggest that work may need to be done with GPs, to increase their understanding of eating disorders beyond the physical symptoms – again, specialist services may be best placed to undertake such work.

Study limitations

While the differences between the specialist and non-specialist care pathways found in the present study are striking a degree of caution is needed as we do not know the extent to which this will generalise beyond London., as there are some important ways in which the study area differs from the rest of the UK. The most relevant is that London contains a considerably higher number of the specialist eating disorders services compared to rest of the country. We do not know what impact this may have on the attitudes of referrers or the confidence clinicians working in generic CAMHS. The finding concerning the differences in the continuity of care are probably most susceptible to the specific conditions in London and may not generalize well to areas with no specialist services.

The study did not include every service that could conceivably accept a referral of an adolescent with an eating disorder, but rather focused on services that handled the large majority of such referrals. While the exclusion of services such as specialist CAMHS targeted at other disorders may have resulted in co-morbid cases being excluded, the study was able to obtain data from most of the eating disorders services, CAMHS that specialised in eating disorders and non-specialist CAMHS in London, with 84% of eligible services providing data. The impact of the different methods of participant identification used by different services is unclear.

While the sample used to test Hypothesis 1 was relatively large, and included cases from the majority of the PCTs in London, the sub-sample of consenters used to test Hypothesis 2 was comparatively small (42.3% of eligible cases) and the analyses of admission rates were underpowered. The logistic regression analyses did not take into account any PCT clusters, so the effect of belonging to an individual PCT on admission was not explored. The differential recruitment rate for specialist and non-specialist services could have biased the sample and influenced the results. However, comparisons between consenters and non-consenters showed no significant differences in the number of services accessed or admissions for inpatient treatment during the study period. Moreover, the findings of high admission rates from general services is consistent with previous reports (30, 349) as is the lower rate in specialist services (359). The short follow-up period for this study is a further limitation, since findings relate only to participants' service use for a year after presentation.

While the results of the qualitative study cannot be taken as representative of a wider population, they suggest a number of ways in which specialist services may be preferable to service users than non-specialist services. These are best described as hypotheses at present, and warrant further study.

Implications for service development and future research

The results of this study are potentially of considerable significance for the way treatment of child and adolescent eating disorders is provided in the NHS. The data suggest that establishing care pathways in which referrals from primary care go directly to specialist outpatient CAEDS could significantly increase levels of case identification while at the same time reducing overall costs by reducing admissions for inpatient treatment and the associated readmissions which are likely to increase cost differentials over time. This study did not

examine the nature of the treatments provided within different services or the impact that specific treatments may have had on outcomes. However, it is likely that part of the explanation of the differences found is a greater use of effective, evidence-based treatments by specialist services. One could argue that a further factor in favour of developing specialist services is that this would facilitate dissemination of such treatments.

The fact that CAED services and specialist CAMHS appeared to be relatively comparable in this study suggests that general CAMHS may be able to achieve similar outcomes to specialist services if they contain some organisation around eating disorders and clinicians have opportunities to develop necessary expertise. The disadvantage of this arrangement, in comparison with specialist eating disorders services, is that developing a truly multi-disciplinary team is often difficult when only a small group of clinicians is involved and such teams are also more vulnerable to the impact of staff turnover (in fact, during the service mapping exercise we heard of several instances when a mini-specialist team was unable to continue when a key member of staff retired or changed jobs).

Conclusion

The study presented here can be considered one of the first stages in the investigation of outcomes following treatment in services with different levels of specialisation in eating disorders. Findings suggest that starting treatment in a specialist outpatient service may have some advantages. Questions remain, however. The difficulty in recruiting participants from CAMHS in particular raises the question of how to evaluate treatment outside of specialist contexts. Future research will need to address this issue.

Chapter 11. Cost of illness and cost-effective treatments (WP7b)

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Abstract

Word count: 250

Background: We aimed to identify services and treatments used by people with AN and associated costs, estimate unit costs of ED treatments, explore cost variations by patient characteristics, explore the economic consequences of AN and estimate the annual costs of AN for England.

Methods: We analysed service use data collected alongside three clinical trials and estimated costs by attaching unit costs to service use. Individual variations in costs were explored using regression analyses. Unit costs of ED treatment and service costs for a cohort of young people with AN over one year were estimated using data from the Care Pathways Study. Economic consequences of AN in adulthood were analysed using BCS-70 data, comparing women with lifetime AN to women without eating problems. Combining publicly available data and results from the ARIADNE studies, we estimated the annual costs of AN in terms of health service costs, private health care costs, benefit receipt and Years of Potential Life Lost.

Results: Service costs were driven by hospital admissions, costs vary by age, illness severity and treatment history. Those treated in non-specialist outpatient services incurred higher costs than those treated in specialist services only, with no differences in outcome. Women with lifetime AN were more likely to be long-term sick or disabled in adulthood, receive benefits and have completed a degree, with no differences in weekly income or employment status compared to cohorts with no eating problems. The annual costs of AN for England were estimated to be between £45m and £230m in 2011.

Introduction

Even though it is clear that anorexia nervosa (AN) has a severe impact on the health care system and people's lives – including patients, their carers, families and partners – to date there have been few attempts at quantifying the economic impact in monetary terms (113, 362). The implementation of cost-effective alternatives to inpatient treatment across the country should be a priority to ensure equitable access and adequate treatment (26, 363, 364). Economics evidence can facilitate this by providing a sound 'cost of illness' estimate, and associated cost-effectiveness analyses, that allow service providers and planners to estimate the monetary benefit of implementing evidence-based services.

This chapter, therefore, attempts to provide some answers to the following questions:

- What services and treatments do people with AN use?
- What are the unit costs of various ED treatments?
- What are the costs associated with service use by people with AN?
- Do costs vary by participant characteristics?
- What are the economic consequences of AN?
- What are the annual costs of AN for England?

The work was carefully integrated with other studies in the programme and therefore depended on data from other WPs being available. During the first phase of the project, a review of the service use, cost and cost-effectiveness evidence was undertaken, informing the data framework for the cost of illness study. The literature review also revealed that little evidence on the economic consequences of AN was available, and a study of the British Cohort Study was designed to fill this gap.

In this early phase, we also designed instruments that would facilitate cost estimation within three RCTs (MOSAIC, CASIS and iMANTRA studies, *Chapters 4, 6 and 8*). The Client Service Receipt Inventory (152), originally devised in 1986, is used to record information on participants' use of services and was carefully adapted in the light of the research questions, service context and participants. A self-report measure was selected as participants were likely to use a wide range of services and there is no one central source of service use data across different agencies (152). GP records, for example, are an unreliable source for data on hospital and community services (365), but there is high agreement between GP records and self-reported GP contacts (366).

We analysed the baseline service use and costs of people recruited to three RCTs (Study 1) and the costs of ED treatment provided in four London PCTs (the Care Pathways Study; Study 2). We also present here our analysis of economic outcomes associated with AN based on the British Cohort Study (Study 3) and our estimate of the annual costs of AN for England (Study 4).

Study 1: Service use and costs associated with anorexia nervosa

Little is known about the service use and costs associated with AN. A recent review of the costs associated with ED and the cost-effectiveness of treatments up to 2010 (362) identified just three partial cost-of-illness studies for AN, and none were based in the UK.

There was only one full cost-effectiveness analysis (352, 367). This compared the costs and outcomes of inpatient treatment, specialist outpatient treatment and treatment as usual and found that specialist outpatient treatment had a higher probability of being cost-effective (up to ca. 60%). One limitation of this study was that only 65% of patients adhered to the allocated treatment.

Our search also identified one study that modelled the value for money generated by different types of ED services in Sheffield, based on cost data provided by the Primary Care Trust (PCT) and using a narrow cost perspective (368). Potential savings to the PCT from preventing admissions were particularly high for residential units out of area or in the private sector at an average of £60.7k per case. The authors recommended that a new commissioning strategy should invest in services that reduce costly inpatient admissions.

Given the paucity of evidence regarding service use, costs and cost-effective treatments, our service use data collected alongside the MOSAIC (127) (*Chapter 4*), CASIS (202) (*Chapter 6*), and iMANTRA (*Chapter 8*) trials is an important addition to the UK evidence base. Here we present the baseline data collected from patients before receiving any of the trial interventions, exploring patient service use and associated costs (three trials), as well as predictors of total service costs (MOSAIC and CASIS).

Methods

Service use

Participants completed the Client Services Receipt Inventory (CSRI, 152) at baseline. The schedule covered a retrospective six-month period and was adapted for each study to include

hospital services, specialist mental health services, primary care services and community based services such as social work and alternative therapy alongside demographic information and details on employment.

Service costs

The costs of service use for each participant were calculated by identifying an appropriate unit cost and duration for each service contact and multiplying these by the number of contacts each person reported. For most hospital, mental health and primary care services as well as social work, unit costs were drawn from publicly available sources (369, 370). Others were taken from previous studies or estimated using an equivalent method (371) from data collected as part of the Care Pathways Study (see Section 2 below). Where service contacts were reported but the number of contacts was missing, the mean for all people in contact with that particular service was entered.

Outcome measures and sample characteristics

Some of our analyses use socio-demographic information and outcome measures collected at baseline in each study. These are described fully in the chapters reporting the outcome findings for each study (*Chapters 4, 6 and 8*).

Data analyses

Service use by participants for the 6-month period prior to the baseline assessment are described in terms of the number using a service or providing a type of care and the percentage of the sample. Service costs are presented as means with standard deviations and ranges by service category.

The relationship between costs, patient characteristics and outcome measures was explored using a cost function approach (372, 373). The aim was to identify if any particular characteristics of people with AN raised or lowered costs as this may influence our cost of illness model. Total service costs are used as the dependent variable, with patient characteristics and measures of clinical severity as explanatory variables in a regression-type framework. To account for the skewed distribution of cost data, regression analysis was performed with 10,000 bootstrap replications and clustering within individuals to obtain robust standard errors. Predictors of costs that were statistically significant were selected and a multivariate model was fitted by stepwise removal of non-significant predictors from a full model. A 90% confidence interval was chosen to determine statistical significance because in

economic analyses, there is less risk associated with type II errors than, for example, in clinical studies. Within our set of potential predictors, there are several sets of variables that are closely related: duration of illness and age of onset, for example, are related to age in opposite ways (i.e. age minus duration of illness is age of onset). Similarly, the highest level of education or qualification achieved will be related to age, and the EDE-Q global score is by definition correlated with its sub-scales. These sets of predictors typically cannot be fitted into the same model, but do give us several options for the final model. In presenting results, we selected the variables that explained the highest proportion of variance while retaining basic principles of parsimony and sense.

Results

Service use

Table 37 shows the number and percentage of participants in each trial using each type of service. Participants reported the highest contact rate with GPs for their EDs in CASIS, followed by outpatient services and dentists, while in MOSAIC, the highest percentage of participants was in contact with outpatient services, followed by GPs for EDs and for other reasons. In iMANTRA, where participants were recruited from an inpatient population, the high use of inpatient services was followed – by a wide margin – by GPs for EDs and psychiatrists / psychologists.

Table 37: Service use for the six month period prior to baseline assessment (3 trials)

Service	MOSAIC		CASIS		iMANTRA	
	Number using	Percent using	Number using	Percent using	Number using	Percent using
Inpatient ED	11	8%	78	50%	41	100%
Inpatient other reason	15	11%	24	15%	1	2%
Outpatient ED	126	89%	88	56%	0	0%
Outpatient other	34	24%	22	14%	0	0%
A&E ED	27	19%	50	32%	2	4%
Psychiatrist*	32	23%	51	33%	7	15%
Psychologist*	28	20%	64	41%		
CPN	17	12%	40	26%	0	0%

Psychotherapist	10	7%	25	16%	0	0%
Family therapist / MFDT	0	0%	7	4%	4	9%
Individual therapist / CBT	2	1%	0	0%	4	9%
CAMHS / AMHS	1	1%	3	2%	3	7%
Crisis team	0	0%	4	3%	1	2%
Residential rehabilitation	1	1%	0	0%	0	0%
GP ED	124	88%	134	86%	6	13%
GP other	96	68%	55	35%	3	7%
Practice nurse ED	32	23%	72	46%	4	9%
Practice nurse other	38	27%	32	21%	0	0%
Other community nurse	6	4%	13	8%	0	0%
Dentist	67	48%	86	55%	4	9%
Optician	36	26%	50	32%	4	9%
Dietician / nutritionist	11	8%	9	6%	5	11%
Counsellor	28	20%	44	28%	0	0%
Alternative therapist	10	7%	22	14%	0	0%
Solicitor / lawyer	7	5%	7	4%	0	0%
Physiotherapist	2	1%	1	1%	1	2%
Occupational therapist	1	1%	2	1%	0	0%
Osteopath	1	1%	0	0%	0	0%
Police	0	0%	0	0%	1	2%
Self-help / support group	13	9%	22	14%	0	0%
CAB	8	6%	12	8%	0	0%
Helplines	15	11%	16	10%	0	0%
Websites	3	2%	2	1%	0	0%
Social worker	9	6%	18	12%	1	2%
Outreach/family support worker	4	3%	7	4%	0	0%
Family centre	0	0%	0	0%	1	2%
Carer	0	0%	1	1%	0	0%

* in iMANTRA, these professionals were combined in one question

Service costs

Table 38 shows the costs associated with service use, summarising the service use data presented in *Table 37* into service categories. Reflecting the pathways of recruitment and the location of the interventions to be evaluated in the RCTs, average costs per person were highest for inpatient treatment in iMANTRA and CASIS, while outpatient treatment costs were the largest contributor to total costs in MOSAIC.

The proportion of total cost absorbed by each cost category for each study can be seen in *Figure 8*, *Figure 9,* and *Figure 10*. Total costs over the 6 months prior to baseline were highest for the iMANTRA group in which all participants had used inpatient care over the previous six months; hospital costs accounted for 99% of total costs. In the CASIS group, who were also recruited from an inpatient population, hospital costs still accounted for 85% of total costs, and only around 6% of this was due to outpatient visits, used by over 60% the participants. In the MOSAIC group – recruited through outpatient services – only 16% reported a hospital admission in the six months prior to the intervention. For all three studies, community, self-help and social work services contributed a very small proportion to total costs even though some of these services were used by over 10% of the study samples.

Table 38: Costs per person by service category (3 trials)

Service category	CASIS			MOSAIC			iMANTRA		
	Mean £	SD	Range	Mean £	SD	Range	Mean £	SD	Range
Hospital	21,045	30,370	0-215,172	4,547	14,403	0-87,794	81,304	12,029	21,672-87,651
Mental health	1,687	2,261	0-11,232	709	1,564	0-11,458	1,062	2,894	0-13,224
Primary care	1,650	1,409	0-7,360	1,046	1,304	85-12,272	229	493	0-2,076
Community services	286	489	0-1,752	115	247	0-1,460	3	16	0-105
Self-help and advice	32	99	0-673	59	394	0-4,500	0	n/a	n/a
Social work	95	397	0-3,780	70	383	0-3,549	49	293	0-1,872
Total costs	24,795	31,121	318-224,025	6,546	15,316	138-96,287	82,647	11,296	25,200-95,124

Note: Hospital includes: Inpatient, outpatient, A & E. Mental health includes: Psychiatrist, psychologist, CPN, psychotherapist, family therapist, MFDT, individual therapist, CBT, CAMHS, AMHS, crisis team, residential rehabilitation. Primary care includes: GP, practice nurse, community nurses, dentist, optician, dietician / nutritionist. Community services includes: Counsellor, alternative therapy, solicitor / lawyer, physiotherapy, occupational therapy, osteopathy, police. Self-help and advice includes: Self-help group, support group, CAB, helplines, websites. Social care includes: Social worker, outreach worker, family support worker, family centre, carer
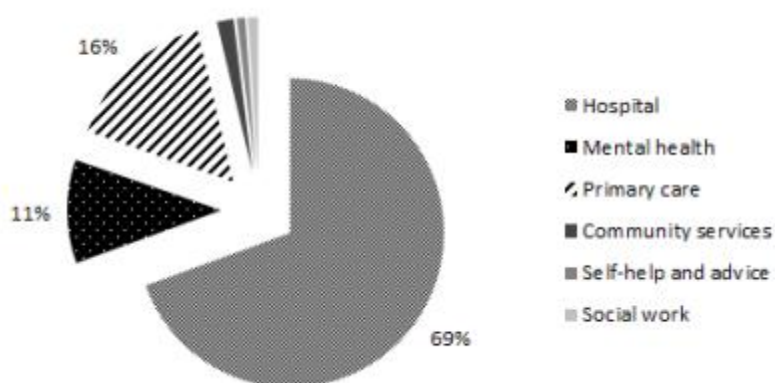
Figure 8: Distribution of costs by service category – MOSAIC
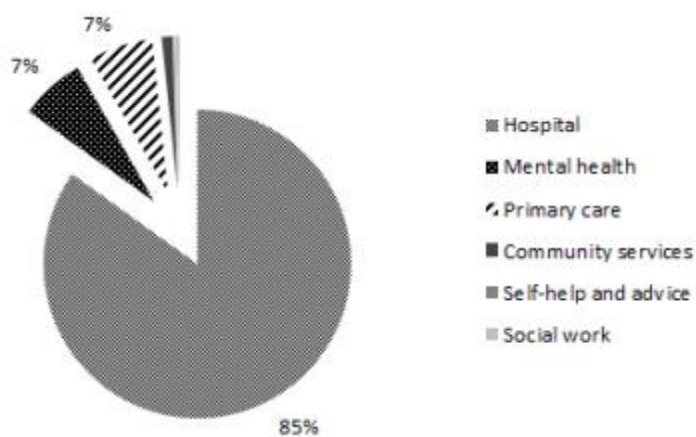
Figure 9: Distribution of costs by service category – CASIS
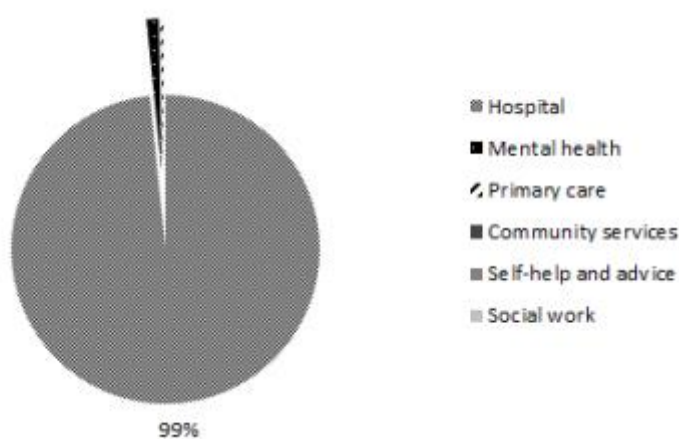
Figure 10: Distribution of costs by service category – iMANTRA

Predictors of service costs

We explored predictors of service costs in the MOSAIC and CASIS groups. *Table 39* and *Table 40* show the results of univariate regression models, relating participant characteristics to total costs, as well as a 'full' model which maximises the proportion of variance in total costs explained (R-squared).

Discussion

The data presented were taken from three studies each with a different recruitment pathway. This was reflected in both the service use data and the costs, as, for example, all participants in iMANTRA reported inpatient stays. The MOSAIC group, recruited through outpatient services, was the most diverse in terms of the range of service use, and also reported the lowest average costs.

We found that factors associated with poor outcomes in AN (374), such as low BMI, higher age and longer duration of illness, were also associated with higher treatment costs. These findings suggest that those people with the highest needs in these domains are receiving the most intensive service response when presenting to secondary or tertiary care.

There were some differences between the studies. Higher age was associated with slightly lower treatment costs in MOSAIC. Previous treatment (number of previous hospital admissions in CASIS and a binary indicator of previous hospital admissions in MOSAIC) were associated with higher treatment costs. Interpretation is difficult, as it is unclear whether this simply reflects treatment costs immediately prior to the study, or a prolonged engagement with services due to severity or chronicity of AN.

English as a first language was also associated with higher treatment costs in CASIS, which may point to differences in treatment uptake among minority population groups (356) – but this is not reflected in a significant cost impact of the 'ethnicity' variable.

Table 39: Predictors of total service costs (CASIS)

Predictor	Univariate models			Full model		
	Coef.	se	p	Coef.	se	p
Constant				39,138	22,154	0.077
Age	-118	235	0.615			
Gender male	7,615	9,121	0.404			
Ethnicity (Other vs White British)	3,054	15,637	0.845			
English is first language	21,426	28,11	<0.001	18,685	5,939	0.002
Cohabiting	1,998	5,033	0.691			
Has children?	-11,184	5,060	0.027			
Number of children	-4,783	1,879	0.011			
Years of education	704	996	0.480			
Degree vs no degree	-4,790	2,696	0.076			
Employment	-6,288	6,376	0.324			
	-2,397	6,343	0.706			
Diagnosis AN vs other	-17,193	3,836	<0.001			
BMI (baseline)	-1,010	951	0.288			
Lowest BMI ever	-4,640	1,567	0.003	-4,816	1,747	0.006
Age of onset	-635	681	0.096			
Duration of illness	-27	18	0.138			
WHO quality of life rating	7,929	5,025	0.115			
WHO health rating	13,206	4,812	0.006	12,932	5,603	0.021
Depression score	355	264	0.178			
DASS anxiety score	287	193	0.137			
DASS stress score	614	171	<0.001	596	189	0.002
Total DASS	179	73	0.015			
EDEQ-Restraint	17	1,203	0.989			
EDEQ-Eating concern	1,835	2,057	0.372			
EDEQ-Shape concern	714	2,346	0.761			
EDEQ-Weight concern	1,665	1,713	0.331			
EDEQ Global score	1,239	1,861	0.505			
Number of hospitalisations	3,723	1,246	0.003	2,747	1,143	0.016
Adjusted R^2						*0.24*

Table 40: Predictors of total service costs (MOSAIC)

Predictor	Univariate models			Full model		
	Coef.	*se*	*p*	Coef.	*se*	*p*
Constant				11,917	3,725	0.001
Age	-243	137	0.075	-303	125	0.015
Ethnicity (Other vs White British)	3,142	3,586	0.381			
Living with partner	-3,371	1,693	0.047			
Degree vs no degree	-4,790	2,696	0.076			
Diagnosis AN vs other	-5,563	1,781	0.002	-3,980	1,718	0.021
BMI (baseline)	-850	614	0.166			
Age of onset	-317	147	0.031			
Duration of illness	-23	99	0.815			
EDEQ-Restraint	-1,448	1,306	0.271			
EDEQ-Eating concern	617	847	0.466			
EDEQ-Shape concern	-401	1,005	0.690			
EDEQ-Weight concern	-965	881	0.273			
EDEQ Global score	-850	1,305	0.521			
Previous hospital admission	16,254	5,137	0.002	16,564	6,882	0.016
Previous treatment for AN	5,120	2,018	0.011			
Taking antidepressants	5,433	2,543	0.033			
Adjusted R^2						*0.23*

<u>Study 2: Economic analysis of the Care Pathways Study</u>

Treatment for severe AN often relies on costly inpatient care (375). In a census of inpatient beds in 1999, 20% of all child and adolescent beds were taken up by ED patients (31), and ED admissions have the longest median length of stay of all adult psychiatric admissions (28). More recently, in the UK there has been a shift from inpatient to outpatient treatment, driven by a shift in treatment philosophy and to halt the flow of money from the public to the private sector, which provided over 80% of inpatient units in 1998 (31, 376, 377). However, little is known about the pathways through care in outpatient services, the associated costs, outcomes and cost-effectiveness.

To help address this evidence gap, the Care Pathways Study (356) (*Chapter 10*) examined the care pathways for adolescents aged 13-18 with AN across 4 PCTs in the Greater London Area. The economic component of this study aimed to attach costs to the treatment received in each care pathway. To this end, the costs of different types of outpatient treatment sessions were calculated based on the information available from the Care Pathways Study service mapping exercise. These unit costs were then applied to each instance of service use of a cohort of young people with AN to facilitate calculating individual-level costs of care by care pathway. In addition, the study explored the types of ED treatments provided in different services, the professionals providing them and variation in individual-level treatment costs by participant characteristics and care pathway. We also calculated the cost of a 'good outcome' based on the Morgan-Russell criterion (187) for each pathway.

Methods

Treatment costs (service level)

The information relevant to the economic analysis was compiled from the service-level questionnaires. The cost of providing treatment was calculated for each service individually and an average for each group of services (specialist ED service – including child and adolescent services and adult ED services, CAMHS with ED specialisation and non-specialist CAMHS). Private sector services were excluded from the economic analysis as the main study focussed on the public sector, and costs of private sector provision cannot be estimated reliably. For each type of staff member, a unit cost was calculated based on their likely Agenda for Change pay grade, working hours, ratio of client contact to other tasks and overheads based on service location (community or hospital), drawing on a compendium of public sector unit costs (369) and using a long-run marginal opportunity cost approach (378).

Individual-level service use and costs

The patient-level data were re-entered to better suit the needs of the economic analysis, showing not just the total number of service contacts for each person, but also what specific service provided each treatment session.

Appendices 3.1 and 3.2 show the data available to the economic analysis in more detail.

Data analysis

At the *service level*, we present the number and percent of services within each service category providing each type of treatment and the type of staff involved in the most commonly provided treatments. Differences in the odds that a treatment was provided or a professional provided a treatment were tested for statistical significance using univariate logistic regression models. Differences in the number of treatments were tested using simple regression models (equivalent to a *t*-test), while differences in the cost of treatments between services were investigated using regression models with 10,000 bootstrap replications.

At the *individual level*, the number of participants from each care pathway receiving each type of treatment is shown. The unit costs (calculated from the service-level information) were then applied to the number of contacts reported for each participant to arrive at individual treatment costs over the one year period. The unit costs of outpatient treatment, summarised by service type to match the types of outpatient sessions recorded in the individual-level data set, are shown in *Appendix 3.3*. These averages were used to estimate the cost of treatment for patients who were in contact with services that were not taking part in the study, based on degree of service specialisation. Unit costs for several other treatments were drawn from publicly available sources (369, 370). These unit costs are shown in *Appendix 3.4*

Results

Sample characteristics

Table 41 shows patient demographics, baseline diagnosis, clinical characteristics and distribution between care pathways for the entire cohort (*n* = 90). Categories with at least five participants in the cell were considered in the analysis of cost variations.

Table 41: Patient characteristics (full sample)

		n of *n* = 90	%
Demographics	Female	87	97%
	White British	62	69%
Parents marital status	Married or cohabiting	70	78%
	Other	20	22%
Living situation	Living with parents	79	88%
	Other	11	12%
Baseline diagnosis	Anorexia	40	44%
	EDNOS-AN	50	56%
Clinical characteristics (baseline)	Other medical condition	11	12%
	Taking psychiatric medication	5	6%
	Any co-morbid psychiatric condition	27	30%
	Co-morbid depression	20	22%
	Co-morbid OCD	1	1%
	Co-morbid anxiety	6	7%
	Self-harm	6	7%
	Previous outpatient treatment for ED	4	4%
	Dietary restriction	33	37%
	Bingeing	9	10%
	Vomiting	21	23%
Care Pathway	Specialist-specialist	53	59%
	Non-specialist-specialist	16	18%
	Non-specialist-non-specialist	15	17%
	Private services	6	7%
	Good outcome at follow-up	32	36%
		Mean (*SD*)	Range
Age (years), *n* = 90		15.1 (1.21)	12-17
Duration of illness (months), *n* = 87		8.1 (7.98)	0-36
Baseline weight / height, *n* = 88		82.8 (10.37)	63-132

Table 42: Treatments provided and cost of treatment, by service type

	Specialist CAEDS incl. other ED services (*n* = 5)			General CAMHS with ED specialisation (*n* = 6)			CAMHS without ED specialisation (*n* = 15)		
	Number providing (%)	Mean £ (*SD*)	Valid *n* (cost)	Number providing (%)	Mean £ (*SD*)	Valid *n* (cost)	Number providing (%)	Mean £(*SD*)	Valid *n* (cost)
Assessment	5 (100%)	152.79 (49.53)	5	6 (100%)	208.75 (51.86)	6	15 (100%)	152.48 (67.99)	13
CBT	5 (100%)	135.52 (20.84)	5	6 (100%)	170.72 (26.46)	6	10 (67%)	163.85 (42.28)	9
PDT[a]	3 (60%)	123.91 (10.24)	3	3 (50%)	129.82 (n/a)	3	5 (33%)	137.12 (13.91)	5
Nurse Counselling	3 (60%)	90.60 (n/a)	2	1 (17%)	71.27 (n/a)	1	3 (20%)	82.09 (n/a)	2
Other indiv. therapy	2 (40%)	129.82 (n/a)	1	2 (33%)	186.17 (n/a)	1	5 (33%)	120.82 (n/a)	1
Group w/o parents	2 (40%)	40.31 (11.69)	2	0 (0%)	n/a	0	0 (0%)	n/a	0
Other group therapy	1 (20%)	n/a	0	0 (0%)	n/a	0	0 (0%)	n/a	0
IFT[b]	5 (100%)	204.67 (37.63)	4	6 (100%)	242.26 (86.03)	6	12 (80%)	246.05 (99.51)	8
MFT[c]	1 (20%)	525 (n/a)	1	2 (33%)	525 (n/a)	1	2 (13%)	525 (n/a)	1
Other FT[d]	1 (20%)	n/a	0	1 (17%)	21.55 (n/a)	1	2 (13%)	129.54 (n/a)	2
Refeeding	2 (40%)	n/a	0	2 (33%)	n/a	0	3 (20%)	n/a	0
Dietary	5 (100%)	40.55 (18.55)	4	5 (83%)	38.95 (10.78)	3	8 (53%)	108.68 (n/a)	2
(Medical monitoring)	5 (100%)	121.56 (89.19)	2	5 (83%)	73.85 (n/a)	1	10 (67%)	177.91 (77.60)	5
Other	1 (20%)	n/a	0	3 (50%)	115.79 (n/a)	1	0 (0%)	n/a	0

[a] Psychodynamic psychotherapy, [b] Individual family therapy, [c] Multi-family therapy, [d] Other family therapy
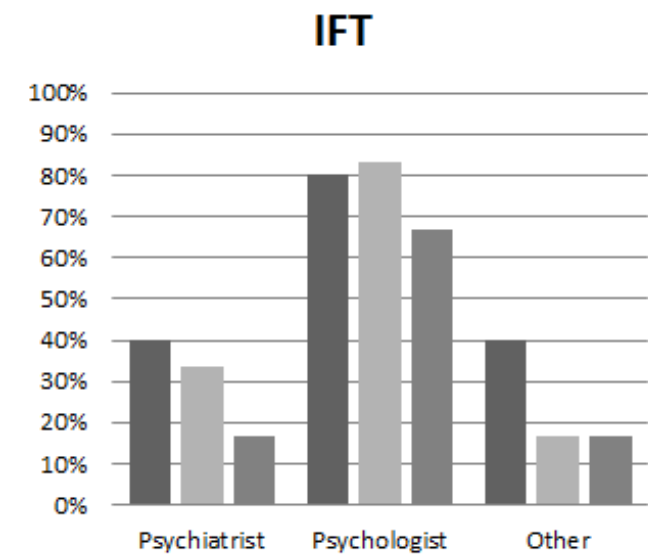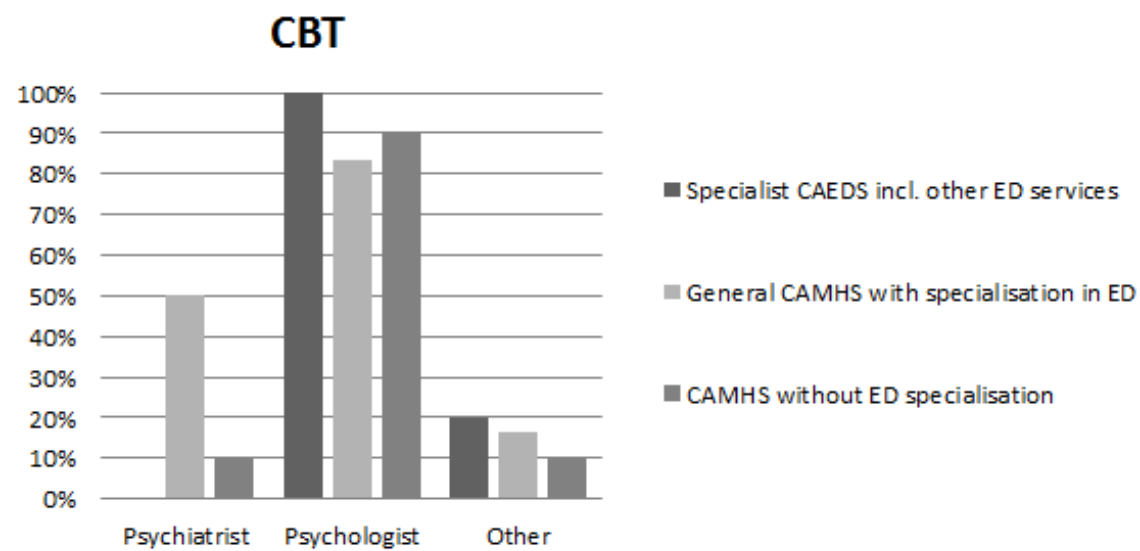
Figure 11: Professionals providing treatment by service type

Treatments for anorexia nervosa offered in outpatient services

Table 42 shows the number of services in each service category that delivered the various treatments for AN (left-hand column) on an outpatient basis. It also identifies the average costs for each treatment.

Across all services, cognitive behavioural therapy (CBT), individual family therapy (IFT) and dietary advice are the most commonly provided treatments. There are differences in average cost per CBT session between service types which are significant at the 90% level ($p = 0.096$), but no significant differences in the average cost of IFT sessions ($p = 0.667$).

The profession and grade of staff delivering the treatment influences the per session cost of that treatment. The percentage of services (by degree of ED specialisation) where specific staff members are involved in providing CBT and IFT are shown in *Figure 11*.

There are no statistically significant differences in terms of delivery of IFT, but psychiatrists are more likely to be involved in CBT in services that are General CAMHS with ED Specialisation compared to non-specialist CAMHS ($p < 0.001$). No specialist ED service reported that psychiatrists delivered CBT.

The number of treatments offered differed significantly between service types. Specialist ED services offered on average 2.6 individual treatments, while specialist CAMHS offered two, and non-specialist CAMHS offered 1.6 ($p > 0.01$). Similarly, specialist ED services offered more than eight different individual psychological or psychiatric treatments in total, while in specialist CAMHS it was seven and in non-specialist CAMHS it was 5.2 ($p > 0.01$).

Unit costs of ED treatment

Table 42 also shows that there is some variation in unit costs (per session) between service types. While a statistical analysis is complicated by the small number of services involved and differences do not reach levels of statistical significance, it is reasonable to conclude that this is due to variations in staff profession (salary) and staff time. In the case of multi-family therapy, specialist services delivered this as whole-day sessions, while in the non-specialist CAMHS the sessions lasted only 60-90 minutes. The high cost of dietetic sessions in non-specialist CAMHS arises because psychiatrists provide dietary advice, while in other types of services it is more likely to be provided by dieticians or nurses who receive smaller salaries. In the case of parent sessions, the variation in unit costs is mainly due to group provision of

sessions for parents in some services (so staff costs per session are shared between several families).

Individual-level service use and costs by care pathway

Patient-level data are available for 84 young people. The main study (see *Chapter 10*) found that 53 of them were assessed in specialist ED services and remained in specialist ED services for treatment (specialist – specialist pathway; S-S). Another 16 were assessed in non-specialist CAMHS and referred to specialist services for treatment (non-specialist – specialist pathway; NS-S), while 15 were assessed in non-specialist CAMHS and remained there for treatment or were directly admitted as inpatients (non-specialist – non-specialist pathway; NS-NS). The details of service use for participants on each pathway are shown in *Table 43*.

Across all care pathways, outpatient single family therapy was the most commonly used form of treatment. In the S-S and NS-NS pathways, the next most commonly used services were individual outpatient therapy and medical outpatient appointments. In the NS-S pathway, the order of individual therapy and medical appointments was reversed.

The costs associated with the service use described above are shown in *Table 44*, again by care pathway. There were differences in the likelihood of admission and in length of stay between the pathways, driving the differences in inpatient costs. Details can be found in House (356) and *Chapter 10*.

The average costs of individual and family outpatient therapy are roughly similar across all pathways, although the average cost of individual outpatient therapy is slightly (but not statistically significantly) lower in the NS-S pathway and the cost of family outpatient therapy is slightly higher in the S-S pathway. Even though dietary advice is a treatment reported to be commonly provided (see Study 3), the cost of dietetic outpatient sessions for this group of young people is low compared to other cost categories.

Table 43: Service use by care pathway

	Full sample (n = 84)		Specialist - specialist (n = 53)		Non-specialist - specialist (n = 16)		Non-specialist - non-specialist (n = 15)	
	n	%	n	%	n	%	n	%
Assessment	84	100%	53	100%	16	100%	15	100%
Individual OP	68	81%	45	85%	9	56%	14	93%
Family OP	82	98%	51	96%	16	100%	15	100%
Multi-family OP	13	15%	8	15%	2	13%	3	20%
Parent only OP	37	44%	23	43%	9	56%	5	33%
Dietic OP	40	48%	26	49%	6	38%	8	53%
Medical OP	52	62%	32	60%	11	69%	9	60%
Telephone calls	52	62%	31	58%	11	69%	10	67%
Psychiatric review	34	40%	22	42%	6	38%	6	40%
Day patient	2	2%	0	0%	0	0%	2	13%
Inpatient (medical)	15	18%	5	9%	6	38%	4	27%
Inpatient (ED)	17	20%	8	15%	3	19%	6	40%

* Medical outpatient appointments include blood tests, bone density scans, pelvic ultrasounds, electrocardiograms and other physical t

Table 44: Service costs by care pathway

	Specialist – specialist (n = 53)		Non-specialist – specialist (n = 16)		Non-specialist - non-specialist (n = 15)	
	Mean £ (SD)	*Range*	*Mean £ (SD)*	*Range*	*Mean £ (SD)*	*Range*
Assessment	170 (36)	112 - 293	151 (43)	98 - 209	152 (40)	98 - 230
Individual OP	1,341 (1,195)	0 - 4,206	955 (1,229)	0 - 3,923	1,933 (1,228)	0-4,414
Family OP	2,976 (2,078)	0 - 8,005	2,998 (2,944)	457-11,786	2,909 (1,135)	965-5,099
Multi-family OP	443 (1,080)	0 – 3,829	479 (1,323)	0 – 4,376	474 (1,149)	0-3,282
Parent only OP	174 317)	0 – 1,509	15 (172)	0 – 591	61 (151)	0-585
Dietic OP	90 (188)	0 – 847	15 (23)	0 – 71	78 (105)	0-382
Medical OP*	2,998 (5,296)	0 - 27,125	4,892 (6,993)	0 - 21,700	2,583 (4,023)	0 – 13,950
Telephone calls	43 (68)	0 – 314	53 (67)	0 – 240	37 (38)	0 - 108
Psychiatric review	1,337 (2,644)	0 - 12,255	784 (1,389)	0 - 5,160	562 (1,166)	0 - 4,515
Day patient	-	-	-	-	1,619 (4,952)	0 – 18,768
Inpatient (medical)	1,529 (6,520)	0 – 34,112	10,260 (22,998)	0 – 79,950	1,421 (2,752)	0 – 8,528
Inpatient (ED)	6,452 (18,073)	0 - 73,308	14,514 (36,791)	0 – 137,760	30,242 (44,199)	0 – 133,824
Total costs	17,544 (28,738)	1,323 - 149,406	35,215 (53,575)	694 -165,656	42,072 (48,277)	3,649 - 168,941
Probability of good outcome	39.6%		31.3%		33.3%	
Cost per good outcome	44,306		112,508		126,342	

*   Medical   outpatient   appointments   include   blood   tests,   bone   density   scans,   pelvic   ultrasounds,   electrocardiograms   and   other   physical   tests
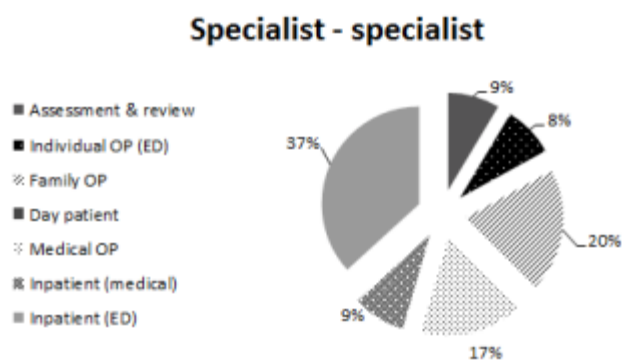
Figure 12: Cost distribution – Specialist-specialist pathway
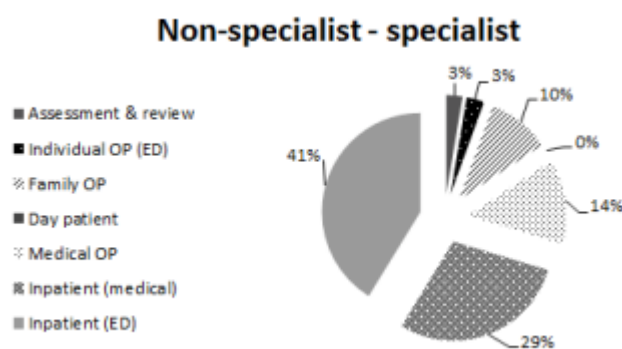
Figure 13: Cost distribution – Non-specialist-specialist pathway
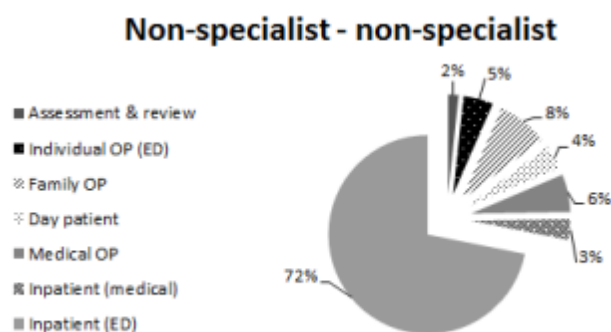
Figure 14: Cost distribution – Non-specialist - non-specialist pathway

Figure 12, Figure 13 and *Figure 14* show the distribution of service costs by care pathway. The largest contributor to total costs for all care pathways are inpatient admissions for ED. This is followed by individual outpatient treatments and the cost of family-based treatments. While inpatient stays due to ED make up a large proportion of costs in the NS-NS pathway, there is a lot of cost variation between individuals (note the large standard deviations), so the difference between pathways is not statistically significant. Similarly, in the NS-S pathway the cost of medical admissions are high but this is at least in part due to two participants with unusually long stays (average length of stay 63 days), and the differences in costs are not statistically significant. Together, ED and medical admissions account for over 70% of total costs in both pathways where the assessment is in a non-specialist service. The lower proportion of costs due to inpatient admissions in the S-S pathway reflects the lower probability of admissions.

Predictors of treatment cost and cost per 'good' outcome

Table 44 shows the total costs over a one year period for each pathway (third row from the bottom). Mean costs were lowest for the SS pathway, and highest for the NS-NS pathway. However, in each case the *SD* is larger than the mean suggesting a wide variation in the total cost of treatment for the participants who followed each pathway.

Table 44 also shows the probability of attaining a good outcome (Morgan-Russell criterion) in each pathway (penultimate row). While the S-S pathway showing the highest probability (39.6%) this was not a statistically significant difference. The final row shows the cost per good outcome for each pathway.

Table 45 shows the results of the univariate regression analysis identifying whether any participants' characteristics are associated with higher or lower total costs. Costs were positively associated with age and duration of illness (significant at the 90% level), and negatively associated with having another medical condition. There were significant differences by care pathway as a whole, and in pairwise comparisons between the S-S and the NS-S pathway ($p = 0.088$) and the S-S and the NS-NS pathway ($p = 0.016$). There was no significant cost difference between the NS-S and NS-NS pathway.

Table 45: Predictors of service costs from univariate models

	n	Coef. (contribution to total costs)	SD	p
White British	56	-9,442	7,431	0.204
Parents married or cohabiting	62	5,759	10,317	0.577
Living with parents	70	565	15,466	0.971
Parental social class:				
Class 2	6	3,631	14,965	0.808
Class 3/4	48	-2,121	15,878	0.834
Class >=5	13	26,608	13,405	0.047
Baseline diagnosis EDNOS vs AN	50	-687	12,213	0.955
Other medical condition	11	-19,991	5,833	<0.001
Any co-morbid psychiatric condition	21	-5,117	8,544	0.549
Dietary restriction	29	1,266	9,529	0.894
Vomiting	18	-14,237	7,040	0.043
Intense exercise	39	-1,895	9,028	0.834
Care pathway:				
Specialist-specialist	53	17,474	14,017	0.213
Non-specialist-specialist	16	26,156	13,962	0.061
Non-specialist-non-specialist	15	17,741	4,103	<0.001
	Mean (SD)			
Age (years), n = 81	15.48 (1.2)	-658	379	0.083
Duration of illness (months), n = 79	7.70 (7.3)	-858	507	0.090
Baseline weight / height, n = 80	83.11 (10.4)	-559	458	0.222

Discussion

Across all pathways, inpatient admissions are the main drivers of costs. The composition of total costs is slightly different in the S-S pathway, where individual and family treatments combined account for almost 45% of costs and there are a lower proportion of inpatient admissions.

The service use patterns are reflected in the total costs, with the S-S pathway incurring the lowest total costs and having the highest proportion of cases with good outcome, although only the cost difference is statistically significant. Although there is a difference in costs, caution is needed when interpreting this finding. Given the small sample size and limited data available in addition to the fact that data collected from London-based services is not generalizable to the rest of England, it would not be appropriate to conclude that this means S-S pathways are the more cost-effective option. The data do not allow us to investigate which individual or service-level factors might have contributed to the observed differences in service use and associated costs. In addition, there were missing data both at the service and individual level, so that our findings should be regarded as indicative rather than definitive.

Our analysis of treatment provision indicates that a higher degree of specialisation is related to offering a wider variety of treatments, and specialist services appear to be more likely to provide a specific treatment beyond CBT, IFT and dietary advice. Again caution is advised; given the small number of services, differences are hard to detect. However, our findings regarding the most commonly provided treatments are broadly in line with an analysis of ED services by the Royal College of Psychiatrists (379).

While there were few differences in the type of professionals providing CBT and IFT, the probability that a psychiatrist is involved in providing CBT was significantly higher in general CAMHS with ED specialisation than in other service types. In part this may be because generic CAMHS teams tend not to include psychiatrists (see 369, p. 172-174).

Specialist skills may also be important. Specialist ED services are likely to include more staff with expertise specific to ED, so that staff on lower pay bands (nurses, perhaps) can provide treatments that in specialist CAMHS are more likely to be provided by a psychiatrist. Also, as House (356) remarks, ED specialisation in general CAMHS is often due to a consultant taking a special interest.

While this study makes an important contribution to knowledge about the costs of ED treatment in outpatient services, the small number of services and individuals participating and the focus on one geographical area in south east England limits the transferability of findings to other parts of the country.

Study 3: Economic outcomes of anorexia nervosa in a British cohort

A number of studies as well as data from this programme have shown the importance of inpatient care in treating AN. While there is commonly some on-site education, such long hospitalisations can mean that young people spend long stretches of time out of education (352) . It seems that in the face of severe illness, education often comes second, although it is a concern for parents (380) and seen as an important determinant of quality of life (381).

There is some evidence that the illness does not affect educational outcomes in the longer term: there was no statistically significant difference between young women with AN and their healthy co-twins five years after recovery from AN (382), and a greater proportion of patients admitted to hospital with AN had completed post-secondary education compared to controls (383). In contrast, Patton and colleagues (384) found young people with EDNOS-AN more likely to be not in education or employment than cohort members without ED. However, we are not aware of any study looking at educational outcomes controlling for other characteristics, such as parental socio-economic status.

There is evidence to suggest that the impact of current AN on productivity in adulthood is severe. International studies found that between 21.4% (383) and 35% (385) of women with AN received state benefits. Long duration of inpatient treatment and psychiatric co morbidity were significant predictors of benefit receipt. It is less clear how a history of adolescent AN affects adult productivity.

Our study describes women who have a self-identified lifetime AN recorded in the British Cohort Study (BCS-70). We investigate the economic outcomes associated with AN, controlling for risk factors and socio-economic characteristics, and estimate the size of the effect.

Methods

British Cohort Study (1970)

The British Cohort Study (BCS-70) includes over 17,000 babies born in the UK in one week in April 1970 and is representative of the UK population. Currently, data are available for seven sweeps up to age 38, so people can be tracked well into adulthood. The use of the data for this study has been registered with the Economic and Social Data Service. No formal diagnosis of ED is included in the BCS-70, but at age 30, there is a set of questions about self-reported lifetime ED, age of onset and type of ED.

Inclusion criteria and comparison group

Participants were included if they had answered the question about lifetime ED at age 30 and either reported AN only (anorexia group) or no eating problems (comparison group). Given that very few males reported AN, analysis by gender was not possible and males were excluded from the analysis.

Data analysis

Given the low population prevalence of AN and the often very detailed categories of outcomes recorded in the BCS-70, categorical outcomes were summarised into dummy variables to facilitate analysis and differences in outcomes were tested for statistical significance using Fisher's exact test, which allows statistical tests for cells with a count <5.

We created a propensity score predicting the probability that a participant would report anorexia based on risk factors of lifetime AN identified by Viner and Nicholls (386). This included frequent feeding problems in infancy, maternal psychological morbidity (Malaise score), separation from the mother for more than one month at age five, and child and maternal BMI, under eating, high self-esteem, conduct, hyperactivity and attention problems (teacher report) at age 10.

We then fit logistic regression models – adjusting for the propensity score – to estimate the effects of AN on the following adult outcomes at age 30: economic activity (active vs not); employment-based social class (class I / II vs lower); benefit receipt (yes / no); and weekly income. We also identified the highest level of educational attainment at age 34. The models were estimated using the logit command in STATA v.12 (154) with the vce(cluster) option to reflect the clustering within individuals across several time points typical for longitudinal data, and controlling for risk factors of AN (propensity score). The difference in weekly

income was estimated using a generalised linear specification with a gamma family and log link. Missing values were accounted for using multiple imputation with chained equations and 20 imputations.

Results

Sample

A total of 116 participants reported lifetime AN. Of these, 101 reported AN only, and 96 were women. In the comparison group, there are 5,449 participants. *Figure 15* and *Figure 16* show the distribution of father's or mother's social class at birth of the cohort member (depending on availability) and level of maternal education at age 5. There were no statistically significant differences between those with and without AN.
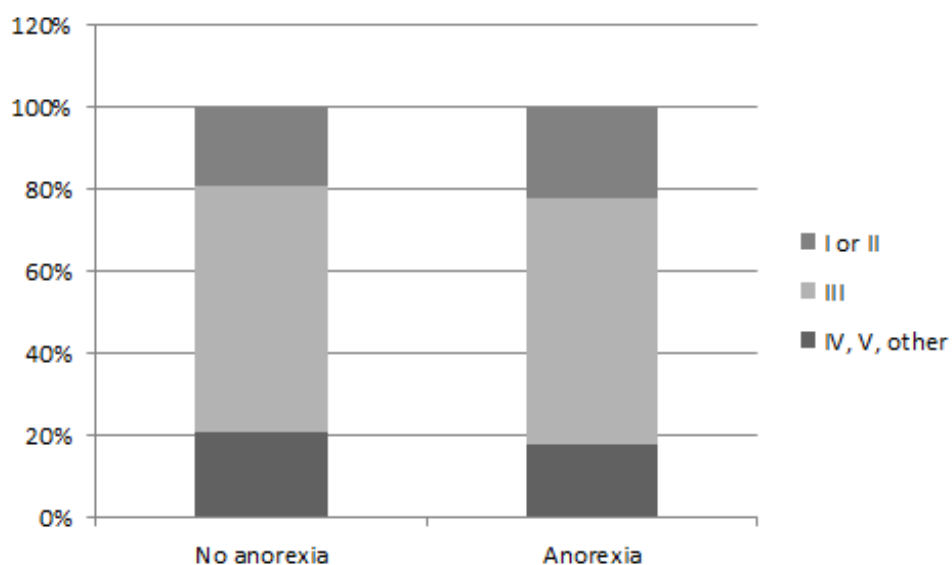
Figure 15: Father's / mother's social class at birth
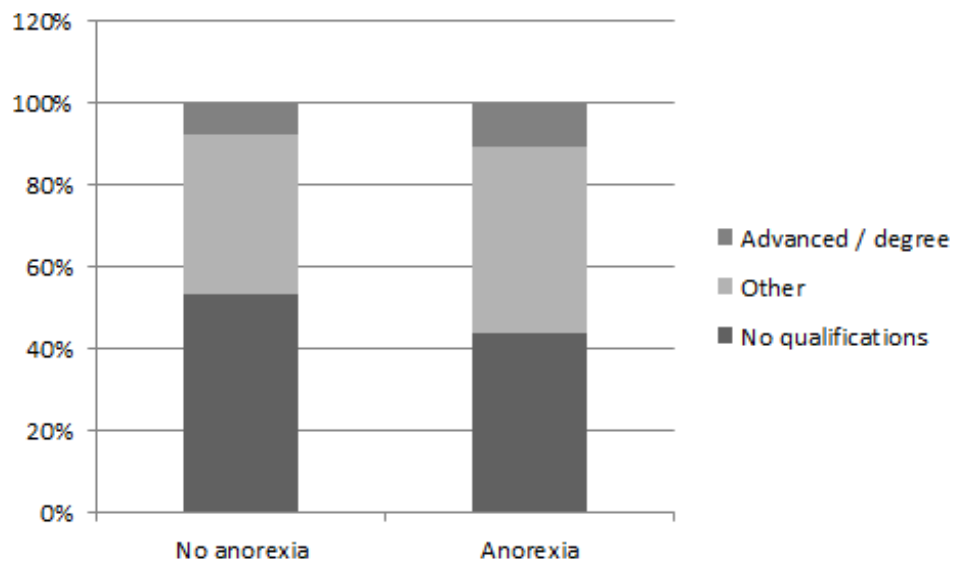
Figure 16: Maternal education age 5

Economic outcomes of anorexia

Table 46 tabulates economic outcomes in adulthood for those with and without AN. "Economically active" was defined as participation in paid employment or in other activities relating to skills and human capital development. There is a statistically significant difference between those with and without AN for three of the eight outcomes. The statistically significant difference in receipt of income-related benefits reflects the higher probability of those with AN receiving income support (17% vs 8%) and housing benefit (17% vs 10%). Mean weekly income at age 30 was £298 for those with and £279 for those without AN, a non-significant difference.

Table 46: Economic outcomes for people with and without anorexia

	No anorexia		Anorexia	
	%	*n*	&	*n*
Economically active vs not	76%	5,449	72%	96
Employed	74%	5,449	69%	96
Sick / disabled*	2%	5,449	10%	96
Full-time work	51%	5,449	48%	96
Class I or II*	40%	4,033	54%	65
Degree vs not*	29%	5,449	35%	96
Receiving income-related benefits*	14%	5,449	22%	96
Family-related benefits	53%	5,449	50%	96

*Difference statistically significant at 95% level

Table 47 shows the odds ratio for each outcome, adjusting for AN risk factors (the propensity score). While there were some significant results, the overall models explain very little variation as expressed by the pseudo R-squared (final column). Those reporting AN were 6.25 times as likely to be long-term sick or disabled. They were also more likely to be in a high social class (I or II; 1.85 times as likely) and have a degree (twice as likely), although these differences were significant at the 90% level only. For those in employment, there was no difference in weekly income.

Table 47: Odds ratios for economic outcomes of anorexia, adjusted for propensity score

Outcome	Age measured	Odds ratio (anorexia)	*p*	pseudo r^2
Long-term sick / disabled**	30	6.25	<0.001	0.016
Employed	30	0.94	0.831	<0.001
Social class I or II if employed*	30	1.85	0.089	0.002
Receives income-related benefits	30	1.01	0.970	<0.001
Has a degree*	34	2.06	0.085	0.003

*Difference statistically significant at 90% level; ** Difference statistically significant at 95% level

Discussion

We found that in those surviving into adulthood, a lifetime occurrence of AN does not appear to affect employment prospects, despite the high hospitalisation rate for treatment. The information about the highest level of education provides use contextual information; *Table 46* shows that 35% of the women in the BCS-70 with lifetime AN had a degree compared to only 29% of those without AN. However, as highest level of education was available for age 34, it could not be used when estimating the probability of being employed at age 30. Having a degree likely increases the chance of employment, leading to the expectation that employment rates should be higher for people with AN. Unfortunately, this relationship cannot be investigated with the data at hand. Similarly, given the higher level of education, a higher weekly income would be expected for those with AN.

In addition to these structural problems, there are issues with data reliability concerning the wage variable. These have been addressed by Dearden and colleagues (387), but some unlikely values remain. While sometimes concerns are raised about the reliability of self-reported diagnoses, simple questions such as the ones used in the BCS-70 have been shown to be as good as more elaborate screening instruments in identifying ED in community samples (388).

The findings from this analysis add to the scant evidence base on the economic circumstances of people with AN and the potential adult consequences of a severe disorder. As more data 'sweeps' from the large cohort surveys become available, the relationship between educational attainment, employment and income for those with lifetime AN can be investigated further.

Study 4: Societal costs of anorexia nervosa

The final analysis presented here brings together the various strands of WP7b. We draw on our review of existing literature, data collected alongside the RCTs and the Care Pathways Study as well as our analyses of the BCS-70 to present an estimate of the annual costs of AN for England.

A recent review of the societal costs associated with ED and the cost-effectiveness of treatments (362) identified several international cost of illness studies, but none included a comprehensive estimate of outpatient service use or wider service use by patients with AN. An early study of the cost of EDs in the UK (389) adopted a health service provider

perspective and used data from the 3rd National Survey of Morbidity in General Practice and the Hospital Inpatient Enquiry to estimate service use in general practice, inpatient bed days and prescriptions. Outpatient treatment and intangible costs were not included. The total cost to the NHS was estimated at £4.2m per annum.

The King's Fund (390) estimated the service cost and lost employment due to AN in the UK. Based on the Hospital Episode Statistics (HES), the cost of inpatient care was estimated to be £2.5m for people under age 15 and £8m for people aged 15-34. The cost of outpatient treatment was derived assuming that only 34.4% of all people with AN are in contact with mental health services (following Hoek and van Hoeken (391)), and that outpatient costs are 41% of inpatient costs (following Striegel-Moore et al (392)), or £4.4m. Lost employment was calculated on the basis that 1,830 people received Incapacity Benefits for EDs. Assuming a weighted annual salary of £19,051, the annual cost of unemployment was estimated at £33m. The total cost was £48m per annum, with 69% due to lost productivity.

More recently, the charity ProBono Economics estimated the annual cost of EDs to be between £1.26 and £9.6 billion (70). This estimate does not distinguish between different types of ED and estimates are to a large extent based on the previous work by the King's Fund, which in turn uses cost ratios from international research to estimate cost categories where English data are lacking. The estimate also includes a burden of disease figure of £950m in the lower-cost scenario, so that only approximately £80m are due to increased health care costs and £230 due to productivity losses.

Our study endeavoured to reduce the reliance on international figures to reflect the structural idiosyncrasies of the English health care context more accurately. We present a conservative estimate based on publicly available data such as the Hospital Episode Statistic and benefit data from the Department for Work and Pensions (DWP). In addition, we present a high cost scenario, incorporating assumptions and results from the literature and the ARIADNE studies. This second estimate includes potential additional admissions and outpatient contacts due to AN recorded under different diagnoses, family (out of pocket or insurance based) expenditure on private sector inpatient provision as well as A & E visits, primary care costs and an estimate of Years of Potential Life Lost (YPLL). Given the limited availability of reliable data sources, we combine top-down and bottom up estimates.

Methods

Prevalence of AN

The likely prevalence of AN by age group was estimated based on recent analyses of incidence in the General Practice Research Database (393) and parameters for the average duration (394) and mortality (67) rates from AN based on a review of the recent literature using the freely available DISMOD II software (www.who.int/healthinfo/global_burden_disease/tools_software/en/).

Costs of AN

The assumptions and data sources used to calculate the societal costs of AN are shown in *Table 48*. Further details can be found in *Appendix 3.5*.

Table 48: Assumptions informing the calculation of the annual costs of AN

Parameter	Assumptions
ED inpatient costs children	1,370 admissions for females with AN (71% of ED admissions)(395)
ED inpatient costs adults	Average length of stay 55.1 days (395)
	37% of FCEs for AN in people < age 18 (396)
Additional inpatient costs	Medical inpatient costs were 29% of ED inpatient costs (Care Pathways Study)
Privately funded treatment	49% of beds provided by the independent sector (379)
	90% of independent beds are NHS funded (31)
Outpatient costs children	110 first appointments (395)
Outpatient costs adults	8,025 subsequent appointments (395)
	78 telephone appointments (395)
Additional outpatient costs	Outpatient costs due to ED account for 38% of inpatient costs (Care Pathways Study)
	Medical outpatient sessions account for 27% of inpatient costs (Care Pathways Study)
A & E	Distribution of treatment assumption
	A & E contacts (CASIS, MOSAIC):
	32% of later inpatients with average 2.5 contacts for ED
	19% of later outpatients with average 1.8 contacts for ED
GP costs	3 visits per person with AN (prevalence based) (70)
Wider primary care costs	Distribution of treatment assumption (24, 395)
	GP (CASIS, MOSAIC):
	86% of later inpatients, average 8.9 contacts
	88% of later outpatients, average 6.2 contacts
	Nurse (CASIS, MOSAIC):
	46% of later inpatients, average 11.3 contacts
	56% of later outpatients, average 6.2 contacts
	Dietician (CASIS, MOSAIC):
	6% of later inpatients, average 6.4 contacts

	8% of later outpatients, average 6.4 contacts
Benefit receipt (lower)	Proportion of benefit claimants attributable to AN vs other ED is the same as the proportion of ED admissions due to AN (71%, (395)) Employment & Support Allowance (ESA); DWP data: 810 claimants per quarter Average weekly amount £90.25 Incapacity Benefit (IB) / Severe Disability Allowance (*SD*A); DWP data: 1,308 claimants per quarter Average weekly amount £56.04
Benefit receipt (higher)	Odds ratio of disability is 6.25 for women with AN (BCS-70 study) Female population of England is 26,974k (ONS figures) ESA; DWP data: 299.6k claimants per quarter → 824 claimants with AN Average weekly amount £76.75 IB / *SD*A; DWP data: 850.3k claimants per quarter →2,399 claimants with AN Average weekly amount £57.39
Potential Years of Life Lost	Life expectancy 82 years (ONS data) 50% of life years lost from Harbottle and Birmingham (397) Discount rate 3.5% Value per life year £30k

Results

Table 49 shows the results of our DISMOD II analysis, estimating a prevalence of approximately 12,000 cases. Combining these results with an analysis by Harbottle & Birmingham (397), we estimate that 9,000 life years are lost to AN each year (discounted to present value; see *Table 49*). *Table 50* shows our low and high estimates for 2010 / 11. Our low estimate shows the annual cost of AN in England to be £45million. At £230million, our high estimate is five times the low estimate with the value of Years of Potential Life Lost absorbing around 60%. In our conservative estimate, nearly 75% of costs are due to inpatient treatment (*Figure 17*). Outpatient treatment accounts for only 3%, or 4% of all healthcare costs. In our high estimate, outpatient treatment accounts for 29% of healthcare costs (*Figure 18*).

Table 49: Estimated prevalence of AN in England

Age group	Incidence	Number new cases	Prevalence	Total cases	% of total cases
10-14	24.0	359	46.1	690	6%
15-19	47.6	773	146.6	2,379	20%
20-24	18.9	337	169.7	3,021	25%
25-29	18.9	346	137.4	2,516	21%
30-34	3.0	53	92.7	1,636	13%
35-39	3.0	53	49.9	882	7%
40-44	1.1	22	27.7	543	4%
45-49	1.1	22	15.3	301	2%
50-54	0.0	0	7.8	135	1%
55-59	0.0	0	3.1	47	0%
60-64	0.0	0	1.2	19	0%
65-69	0.0	0	0.4	5	0%
70+	0.0	0	0.1	1	0%

Table 50: Conservative and high estimate of the annual costs of AN in England (2010/11 prices)

Parameter	Conservative estimate	High estimate
ED inpatient costs adults	£20.9m	£20.9m
ED inpatient costs children	£12.7m	£12.7m
Additional inpatient costs	-	£9.7m
Privately funded treatment	-	£1.6m
Outpatient costs adults	£860k	£13.7m
Outpatient costs children	£610k	£8.1m
A & E	-	£400k
GP costs	£5m	-
Wider primary care costs	-	£7m
Benefit receipt (lower)	£4.9m	-
Benefit receipt (higher)	-	£10.4m
Potential Years of Life Lost	-	£140m
Total costs	£45m	£230m
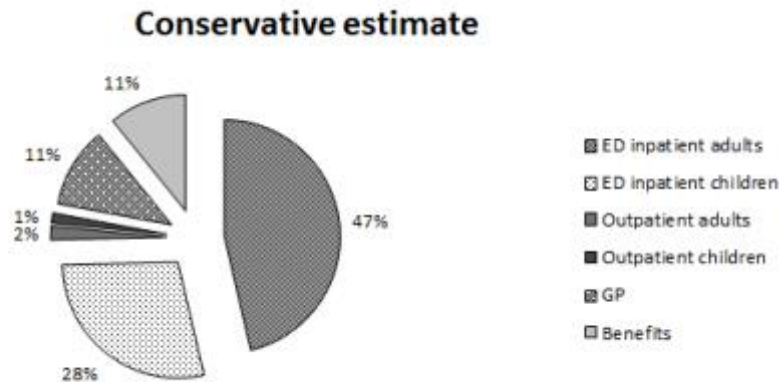
Figure 17: Distribution of costs, conservative estimate
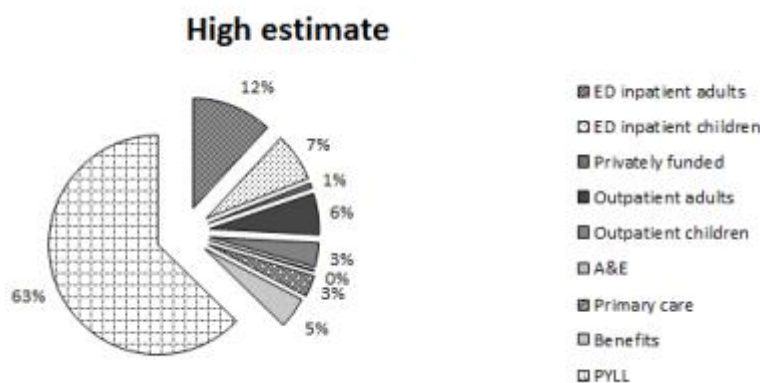
Figure 18: Distribution of costs, high estimate

Discussion

Any study of the social costs of AN is currently limited by poor data availability, in part due to the small number of cases. Assumptions are therefore needed to come up with reasonable estimates. While there are many potential points of contention in our assumptions, a few are likely to have a significant impact on results and are worth discussing.

It is unclear how many people with AN receive treatment and in what setting. Our assumption focusses on the main treatment setting, while in reality, there will be overlaps, with people admitted for inpatient treatment who previously or subsequently receive outpatient treatment, and who may have concurrent input from their GP.

Moreover, it is difficult to account for undetected cases. The "true" prevalence of AN may be 2-3 times as high as estimated from either self-report or within services (398), and it is unclear what the cost implications of this may be. Similarly, we are unable to estimate costs related to sub-threshold AN or EDNOS-AN, as few data are available; there is a tendency to report research findings without distinguishing EDNOS-AN and EDNOS-BN.

Estimating the amount of benefits paid due to AN is difficult despite the availability of DWP data. While the majority of claimants received benefits for five or more years, we may overestimate benefits because the data do not show how many people start or stop claiming benefits within a quarter.

Finally, there are uncertainties surround the data from Hospital Episode Statistics. Data are available by diagnosis, but admissions linked to AN may happen for various reasons, such as cardiac problems, self-harm or other medical problems. Further, the average length of stay reported in HES is much lower than that reported by a recent RCP survey of ED services in the UK (379) which reported a length of stay of over 18 weeks, and a recent study on the duration of stay in UK Specialist ED Units reported an average length of stay of 26 weeks for adults and of 29 weeks for adolescents (218). One possible explanation is that HES conflates stays in psychiatric or ED units (typically for weight restoration or other mental health concerns such as self-harm) and stays in medical or paediatric units often linked to acute medical issues, which tend to be much shorter. In addition, HES data may not be entirely reliable (399). To account for this, we assumed that inpatient treatment may be much more frequent that the diagnosis-based data suggest in our high cost scenario. Given that a high proportion of AN cases is likely treated on an outpatient basis, and given that the number of sessions required is generally high, the small contribution of outpatient costs in our conservative estimate is surprising, and it is possible that there are again issues with the underlying data. We therefore estimated potential additional costs in our high cost scenario.

It is difficult to compare our estimate to the recent work by ProBono Economics (70) because it did not distinguish costs by type of ED. However, some differences are due to different unit costs applied to incidents of service use and differences in data sources. For example, while HES showed around 8,000 outpatient contacts for 2010/11, the ProBono Economics estimate cites unpublished data suggesting the number may be much higher (18,000). Other differences arise from the way private sector healthcare costs were treated. While HES reports data on both NHS beds and NHS commissioned private sector services, the ProBono

Economics estimate assumed the HES data referred only to NHS beds, thus arriving at a much larger figure for additional private costs (£45m vs £1.6m).

Two areas of costs outside the public sector should also be mentioned. While our study of the BCS-70 was unable to show an impact on earnings in adulthood due to a lack of data, there is reason to believe that AN is associated with productivity losses both from absenteeism (time taken off due to illness) and presenteeism (lower productivity when at work due to illness), and that the impact may be large. While no estimate of the reduction in productivity associated with AN is available, Goetzel and colleagues (400) reported an average impairment of daily productivity due to depression, sadness or mental illness of 10.7%. Moreover, with an average length of stay of over 50 days, the impact of hospitalisation on the ability to attend work is clearly severe. These reductions in productivity likely not only affect patients, but also carers and partners, who often experience high levels of psychological distress, depression and anxiety (196).

Informal care costs have also been excluded from our model. It is provided to people with AN by parents, carers and partners. The analysis of data collected in the CASIS study (*Chapter 6*) shows that up to three quarters of carers spent nearly a full day per week providing ED-related care (401) with potential impacts not only on their health and wellbeing but also on their capacity to engage in paid employment.

While we attempted to integrate findings from the ARIADNE studies into our estimate, the limited data available did not allow us to reliably estimate total costs by ethnicity, gender and ED severity, although we did attempt to distinguish costs by broad age group where possible. As more data from the ARIADNE studies and the large cohort studies become available, it may be possible to address the gaps in our estimate highlighted here.

Conclusions

While the research agenda on the economics of AN remains long, findings from this Programme add considerably to the small evidence base for treatment and support of people with AN in England.

What services and treatments do people with AN use?

To address this question we identified services used at baseline by participants in three ARIADNE trials; CASIS, MOSAIC and iMANTRA. There are two central conclusions from

our analyses. First, service use linked to the recruitment path way of each study. The iMANTRA group, for example, were recruited from an inpatient population, thus all of the participants had been in hospital prior to the baseline interview. Because hospital admissions tend to be quite extended for people with AN, use of any other services was low. It is, therefore, important to use such data with caution when making inferences about service use for the wider group of people with AN.

Our second conclusion comes from the CASIS and MOSAIC studies, where participant used a wide range of services and supports. Along with previous studies, we find that inpatient admission is often the mainstay of treatment for AN, but these studies show that outpatient clinics and mental health professionals all provide important components of a treatment package, as does primary care with more than four-fifths of these two samples seeing the GP about their ED and between a quarter and a half seeing their practice nurse. Community, self-help and community services all played a part in supporting a small but significant minority of participants.

What are the unit costs of various ED treatments?

Our analysis of the unit costs of ED treatments comes from the Care Pathways study. The research identified treatments delivered to patients in this cohort from case notes, rather than solely relying on reports from services about what they *could* provide. Cognitive behaviour therapy (CBT) and individual family therapy (IFT) were the most common treatments. Mean per session unit costs for treatment varied considerably. Average unit costs were lowest in the Specialist ED services (£136 for CBT and £205 for IFT) with IFT unit costs similar for the CAMHS with ED specialisation and generic services (approx. £245). Unit costs are sensitive to the number and profession of staff delivering the intervention, as well duration of the session and whether the intervention is provided in a group or individual setting.

What are the costs associated with service use by people with AN?

For the three trials analysed for this chapter mean costs varied, reflecting the recruitment path. However, the range was wide in all studies indicating different intensities of service response. The lowest six monthly cost was just £138 (MOSAIC study participant) and the highest was £224,025 (CASIS participant). In all three studies, hospital services absorbed the highest proportion of total costs – between 69% and 99% of total costs.

A similar wide range can be seen for the participants in the Care Pathways study, which focussed solely on health service treatment for AN. The lowest annual cost was £700 and the highest was £169,000.

Do costs vary by participant characteristics?

The large variation in costs warrants further investigation. Our analysis of cost variations in the MOSAIC, CASIS and Care Pathways data suggest previous treatment history (perhaps a marker for severity or chronicity) is associated with costs, alongside age, first language other than English and co-morbidity. However, none of these equations explained a large proportion of the cost variation and much, as suggested by the findings of previous studies (24, 379), may be related to service availability and pathways to treatment.

What are the economic consequences of AN?

Our study of the BCS-70 suggests that people with lifetime AN who survive into adulthood have a higher probability of being long-term sick or disabled, have completed a degree and be in a high social class if employed. No differences in weekly income could be found, although this analysis was not able to control for highest level of education, severely limiting the conclusions from the study.

What are the annual costs of AN for England?

Our final set of analyses brought together findings from the literature, the three trials, the Care Pathways Study and the BCS-70 study to estimate the societal costs of AN. Our conservative lower-bound estimate suggests an annual cost of AN in England of around £45 million. Seventy-five per cent of this is for inpatient treatment, despite the growing use of specialist outpatient clinics. Primary care and receipt of social security benefits account for a further 10% each. Our high estimate is five times higher at £230 million per annum, with more than 60% absorbed by the value of 'years of life lost'.

Chapter 12.   Overall discussion and conclusions

Ulrike Schmidt and Helen Sharpe

This research programme focused on anorexia nervosa (AN), a perplexing and frightening illness affecting mainly young females. In seven integrated work packages (WP) it aimed to (a) develop and test tools for eating disorder (ED) prevention and early intervention in schools, (b) develop and test targeted, disseminable and cost-effective treatments (first-line, adjuncts to inpatient re-feeding and relapse prevention) for adults with AN, across the spectrum of illness severity and based on empirical models of AN grounded in clinical neuroscience, (c) develop and test targeted, disseminable and cost-effective interventions for carers of adults with AN, (d) better understand perplexing core symptoms of AN (hyperactivity and its psychological and biological correlates) with the aim of informing future intervention development, (e) better understand the needs of particular populations (i.e. mothers with ED and their offspring); (f) optimise care pathways for young people with AN and (g) identify the costs of services used by people with AN and estimate the annual cost of AN for England. Throughout we worked with patients and carers to achieve these aims.

Below, we discuss key findings emanating from the integrated WP in relation to these aims and assess their clinical and research implications. Rather than discussing each WP separately, where appropriate, we have grouped WPs together. A list of the main clinical and research implications emanating from the WPs is also provided in *Table 52* and *Table 53* at the end of this chapter.

Key findings and their clinical and research implications

1. ED-prevention and early intervention in schools (WP1a, WP1b)

A one day training programme on early detection and strategies for managing ED in schools resulted in improved self-reported knowledge, attitudes and confidence of schools staff in identifying and managing ED in an uncontrolled, feasibility study (WP1a). Secondly, a teacher-delivered intervention was feasible and improved risk factors for ED (body dissatisfaction, thin-ideal internalisation and self-esteem) in adolescent girls in a cluster-randomised trial (WP1b).

Together these studies indicate that teachers and other key school staff can be trained to deliver efficacious preventative interventions for ED in schools and to feel more knowledgeable, more positive and more confident in relation to identifying and supporting students with ED. Of note, in both studies, training was brief and fitted in with school staff's work schedules. More research is needed on these interventions before they are widely

disseminated. The teacher training programme outlined in WP1a could best be tested using a fully powered stepped wedge design (402), rather than a randomised controlled trial. Such a study should develop and incorporate objective measures of staff competence in dealing with common ED scenarios relevant to school settings and also demonstrate the impact of the intervention on student outcomes. The teacher-delivered prevention programme developed in WP1b should be tested in a large scale adequately powered cluster RCT to determine the effectiveness of this programme in a range of school environments. This should involve the programme being evaluated for boys as well as girls. Additionally, future research might assess the combination of both interventions in a 'whole school approach' to prevention and early detection and management of ED.

2. Development and testing of targeted, disseminable and cost-effective treatments (first-line, adjuncts to inpatient re-feeding and relapse prevention) for adults with AN (WP2a, WP2b and WP5)

First, a multi-centre trial of two first-line outpatient psychological interventions (MANTRA and SSCM) found both psychological therapies significantly improved ED and other clinical outcomes in outpatients with AN. ED outcomes compare well with those from the only other large scale RCT in a similar population (130). Of note, patients significantly preferred MANTRA to SSCM and found it more credible (WP2a). Second, in a quasi-experimental study in inpatients with AN, the addition of a cognitive-emotional skills training (CREST) to treatment as usual was acceptable with perceived benefits by patients, but it showed no benefits (in relation to ED or other clinical outcomes) compared to TAU (WP2b). Thirdly, a feasibility RCT in AN patients discharged from inpatient treatment, compared the addition to TAU of an email-guided relapse prevention programme (iMANTRA) with TAU alone, and suggested that there are treatment effects of a medium size in relation to a higher BMI and to lower distress in the experimental group at 12 months discharge (WP5).

Findings from the large-scale RCT in WP2a suggest that both MANTRA and SSCM can be recommended as first-line outpatient therapies for adults with AN, with the caveat that currently longer term outcomes for both of these treatments are unknown. Future research should focus on obtaining longer-term (2 and 5 year) follow-up data from the RCT, to determine the relative longer term efficacy of these two psychological treatments. Moreover, mediators and moderators of outcome should be evaluated. To ensure adequate sample size for mediator and moderator analyses, data from the present study can be combined with those

from an earlier pilot RCT (135). Furthermore, given the manual-based nature of MANTRA (including lots of information, education and skills training) a future study evaluating this approach in recent onset/first episode cases of adults with AN may be useful. Finally, MANTRA might also be a useful adjunct to family-based treatments for adolescents with AN.

Preliminary evidence from WP2b suggests that Cognitive Remediation and Emotions Skills Training (CREST) is an acceptable therapy that is valued by patients and clinicians. The preliminary trial in WP5 indicates that iMANTRA is a feasible and safe intervention, which may have promise in the aftercare of inpatients with AN. Thus, both of these interventions should be evaluated further.

For CREST, the next step would be to conduct an RCT to explore benefits of this intervention in comparison to other manualised treatments of similar length. A larger study of the group format of CREST will be also desirable to consolidate preliminary findings.

For iMANTRA (piloted in WP5), the next step would be to carry out a large scale RCT including health economic analyses, longer term follow ups and regular assessments to explore detailed relapse/recovery trajectories. A further study exploring the efficacy of iMANTRA using facilitators that have an established therapeutic relationship with the patient would be helpful to determine if this improves outcomes.

3. Development and testing of targeted, disseminable and cost-effective interventions for carers of adults with AN (WP3)

The large-scale, multi-centre RCT in WP3 shows that the addition of a psychoeducational and skills sharing intervention (ECHO) for carers of people with severe and/or enduring AN to standard inpatient care reduces carer time spent care giving, burden and expressed emotion. In addition, patients had reduced ED symptomatology and improved quality of life at 6 months. These findings show that sharing skills and information with family members benefits carers and patients.

Future research should examine whether adding the carer intervention evaluated in WP3 onto standard outpatient care for adults with AN improves outcomes. Another step will be to examine whether adding a more intensive family intervention (workshops) improves inpatient care.

4. Improved understanding of hyperactivity and its psychological and biological correlates in AN (WP4)

Key findings from this observational study are that people with AN report that they engage in higher levels of activity that healthy controls or people with an anxiety disorder, but that an objective measure (actimetry) shows actual activity levels are similar across in- and outpatients with AN, anxiety disorder sufferers and healthy controls. The study did find that, the drive to exercise is significantly higher in AN patients than in controls and that it is tied to ED pathology and a desire to improve mood.

The difference between actual and perceived levels of activity in people with AN may reflect the fact that their pathological drive to exercise is resulting in them attempting to exercise even when they are physically compromised by illness i.e. at a time when they have significantly less skeletal muscle mass than the control participants. Levels of activity did not appear to be related to endocrine measures, such as plasma leptin or salivary cortisol, or to daily average temperature (i.e. activity is not driven by a desire to keep warm). Taken together with other recent evidence these findings suggest that exercise is driven and rewarding to sufferers with AN (403). It also suggests that clinicians need to develop interventions that address the pathological drive to exercise rather than exercise per se.

5. Improved understanding of the needs of mothers with ED and their offspring (WP6)

WP6 focused on a special population: mothers with ED. Key findings of studies in this WP were that ED are common in pregnancy and they are associated with unplanned pregnancies and fertility treatment. In addition, children of mothers with ED are at risk of growth difficulties and disordered eating patterns. A key implication of these findings is that continuity of care from pre-conception to the post-natal period is paramount for women with ED. Findings from this study have provided data for future intervention development. Future research should focus on developing and testing a tailored intervention for pregnant women with ED, focusing e.g. on giving them information and skills on how to best manage their own nutritional needs during and after pregnancy and the nutritional needs of their off-spring in utero and after birth. In addition, following the children of women with ED into adolescence will be essential for exploring the intergenerational risk of ED.

6. Optimising care pathways for young people with AN (WP7a)

The assessment of care pathways study in WP7a showed that direct access to specialist ED services for young people with AN was associated with higher referral rates, lower admission

rates, greater consistency of care and greater user satisfaction. Thus, there are clear benefits in having specialist community based outpatient services which are easily accessible directly from primary care: they provide good clinical outcomes with markedly lower rates of hospital admissions (and therefore are at considerably lower costs, see *Chapter 11*) and better continuity of care than generic services can deliver. Training in evidence-based treatments should focus on developing skills in specialist multidisciplinary teams.

Future research should evaluate the role of specialist ED services beyond the metropolitan London context using a larger scale study. Further research is also needed to explore the barriers to identifying adolescents suffering from BN as they are poorly identified even in specialist areas, and a high proportion do not receive timely treatment.

7. Estimating the costs of services used by people with AN and the annual cost of AN for England (WP7b)

A key finding from this WP is that being treated in specialist services is associated with lower costs. Secondly, the annual costs of AN in England are estimated at between £45m and £230m. Moreover, the economic analyses in W7b demonstrate that AN is associated with a high risk of adult disability. Effective prevention and early intervention to prevent long-term disability are therefore likely to provide significant patient benefit and cost savings. While inpatient treatment is the largest contributor to treatment costs, participants with AN accessed a wide range of services (primary care, self-help, community services). There may be scope to develop collaborations with community-based services to improve early identification and to ensure appropriate treatment. Future research should include a longitudinal study investigating the impact of AN on education, employment and potential earnings differential. It will also be helpful to gather longer-term follow-ups of clinical trials with accompanying economic evaluation to better reflect the longer-term costs of treatment and to allow us to estimate the incidence-based costs of AN.

Overall strengths of the programme

The strength of the programme is that it took a life-stage and illness stage perspective on a disorder which typically starts in adolescence, but which often continues into adulthood. It was also a highly ambitious programme of great depth and breadth. It included:

- A mixture of well-conducted large-scale adequately powered definitive trials (WP2a: MOSAIC trial, WP3: CASIS trial)

- Studies (including smaller RCTs, quasi-experimental designs and pre-post designs) assessing feasibility of novel interventions (WP1a: School staff training, WP1b: Me, You & Us, WP2b: CREST, WP5: iMANTRA)

- Longitudinal studies producing evidence that can form the basis for future intervention development (WP4: to reduce the drive for thinness and exercise, and WP6: for pregnant women with ED)

- A study assessing care pathways for young people with AN (WP7a)

- Studies on the cost of AN in different settings (WP7b).

Although the programme was led by a team from one unit, many of the studies had multiple collaborating sites (WP1a, WP1b, WP2a, WP2b, WP3, WP4, WP5) from across the UK or across London (WP7a) thereby ensuring broad generalisability of findings.

Most of the WPs used mixed methods including quantitative and qualitative components. The qualitative components were used to either inform intervention development (e.g. WP1b: 87, e.g. WP1a: 404, 405) or as process evaluations of the interventions tested (WP2a: 159, 160, 161, WP2b: 406, WP3: 407, WP7, see Chapter 11). Both approaches have been highly valuable and have added much needed detail to inform the iterative process of intervention development and testing.

The programme has yielded several manual-based interventions for prevention of, training in and treatment of AN and related ED. *Table 51* shows the interventions that have emanated from the programme.

Table 51: Interventions developed as part of the programme

Work package	Name	**Purpose, Setting & Support**
WP1a	Teacher Training Intervention	A one-day manualised training programme to improve teachers early detection and management of ED in schools
WP1b	Me, You and US	Universal prevention for ED in schools focusing on reducing established risk factors and delivered by school staff
WP2a	Maudsley Model of Anorexia Nervosa Treatment for Adults	A manualised outpatient treatment focusing on established maintenance factors for AN delivered by therapists
WP2b	Cognitive Remediation and Emotions Skills Training (CREST)	A manualised treatment focusing on emotion recognition, regulation and social skills in people with severe AN
WP3	ECHO (Expert Carers Helping Others)	An intervention focusing on carers' skills training and combining a self-help manual with DVDs and coaching sessions
WP5	iMANTRA	An online intervention to prevent relapse in severe AN following inpatient weight restoration

Most of these interventions are grounded in our model of AN, underpinned by clinical neuroscience (WP2a, WP2b, WP3, WP5). Testing these interventions has involved using neuro- and social-cognitive measures as outcomes, an approach that is novel in AN treatment studies.

Central to all of the interventions developed and tested here is that they subscribe to the ethos of collaborating with and sharing specialist skills and knowledge with patients, carers and school students and staff. This collaborative approach empowers patients and carers to become experts in understanding and managing their condition.

The interventions developed here can be easily disseminated within schools and the NHS either immediately, or after further research.

Overall limitations

Given the ambitious nature of the programme and the confines of available resources and time, by necessity all of the studies had to make compromises in terms of the size and nature of samples studied, the control samples, number and duration of outcome assessments, and duration of follow-ups. Details of these compromises and limitations are outlined in the relevant chapters of this report.

Conclusions

This programme has focused on development of interventions for prevention, treatment and training in AN and related ED. The results of the programme's studies have important implications for the management of AN (and ED) across the full course of this disorder, from detection through to preventing relapse. Future research is essential to increase our understanding of optimal disease management for AN.

Table 52: Key implications for practice

• The feasibility study in WP1a indicates that in schools, staff knowledge, attitudes and confidence towards ED can be improved by brief face-to-face training. Following further effectiveness testing, detection and management of ED in a school setting may be improved by making this training available to school staff.
• WP1b shows it is feasible to train school teachers to deliver efficacious preventative interventions for ED. How to develop interventions with sufficient flexibility to manage a range of school environments needs further examination.
• The RCT in WP2a shows that at 6 and 12 months post-randomisation both psychological treatments tested (MANTRA and SSCM) significantly improve key clinical outcome measures in outpatients with AN. Patients see MANTRA as more acceptable and credible. Further follow-ups are needed to determine maintenance of treatment effects in the longer term. However, based on available evidence, both treatments can be considered as efficacious first-line outpatient treatments for adults with AN.
• WP2b demonstrates that Cognitive Remediation and Emotions Skills Training (CREST) is an acceptable therapy, valued by patients and clinicians: however, the addition of CREST to TAU is not is not superior to TAU alone. Further work is

needed to establish the benefits of adding CREST as an adjunct to inpatient care.

- The RCT in WP3 shows that addition of an intervention for carers of people with AN to standard inpatient treatment reduces carer time caregiving, burden and unhelpful caregiving behaviours. Patients being cared for by those receiving the intervention show reduced ED psychopathology and improved quality of life. Sharing skills and information with family members is of benefit for patients and carers.

- The observational study in WP4 shows that objectively measured activity levels are not higher in AN: it may however, be problematic because of their poor health. Patients with AN have an increased drive to exercise that is linked to ED pathology and a desire to improve mood. Reducing this drive to exercise should be a treatment objective.

- The pilot trial in WP5 indicates that iMANTRA is a feasible and safe intervention, which may have promise in the aftercare of inpatients with AN.

- WP6 focused on the special population of mothers with ED. The findings show that ED are common in pregnancy and are associated with unplanned pregnancies and fertility treatment. In addition, children of mothers with ED are at risk of growth difficulties and disordered eating patterns. Continuity of care from pre-conception to the post-natal period is paramount for women with ED and interventions designed for this special population may benefit them and their children.

- The assessment of care pathways in WP7a shows that there are clear benefits in having specialist community based outpatient services which are easily accessible directly from primary care as they provide good clinical outcomes with markedly lower rates of hospital admissions (and therefore are at considerably lower costs) and better continuity of care than generic services can deliver. Training in evidence based treatments should focus on developing skills in specialist multidisciplinary teams.

- Finally, the economic analyses in W7b demonstrate that AN is associated with a high risk of adult disability. Effective prevention and early intervention to prevent long-term disability are therefore likely to provide significant patient benefit and cost savings. While inpatient treatment is the largest contributor to treatment costs, participants with AN accessed a wide range of services (primary care, self-help, community services). There may be scope to develop collaborations with community-based services to improve early identification and ensure appropriate treatment.

Table 53: Key implications for future research

- To carry out a fully powered stepped wedge study to test the effectiveness of the school staff training programme developed in WP1a. This research should develop and incorporate objective measures of staff knowledge and confidence and also demonstrate the impact of the intervention on student outcomes.

- To conduct a large scale cluster RCT of the teacher-delivered prevention programme developed in WP1b to determine effectiveness of this programme in a range of school environments. This should involve the programme being evaluated for boys as well as girls.

- To gain longer term (2 year) follow up data from the RCT in WP2a, which are essential to determine the relative efficacy of the two psychological treatments evaluated and the maintenance of treatment gains.   Given the manual based nature of MANTRA a future study of recent onset/first episode cases of AN may be useful.

- To conduct an RCT to explore benefits of CREST (examined in WP2b) in comparison to other manualised treatments of similar length. A larger study of the group format of CREST will be also desirable to consolidate preliminary findings.

- To examine whether adding the carer intervention evaluated in WP3 onto standard outpatient care improves outcomes. Another step will be to examine whether adding a more intensive family intervention (workshops) improves inpatient care.

- To conduct a replication of the work in WP4 in future larger study in patients with AN, using a range of actimetry measures and measuring felt temperature. In addition, studies should be designed to test interventions that target the drive to exercise in AN.

- To carry out a large scale RCT of iMANTRA (piloted in WP5), with economic analyses, longer term follow ups and regular assessments to explore detailed relapse/recovery trajectories. A further study exploring the efficacy of

iMANTRA using facilitators that have an established therapeutic relationship with the patient would be helpful to determine if this improves outcomes.

- To develop and test a tailored intervention for pregnant women with ED. In addition, following the children of women with ED into adolescence will be essential in exploring the intergenerational risk of ED.

- To evaluate the role of specialist ED services beyond the metropolitan London context using a larger scale study. Further research is also needed to explore the barriers to identifying adolescents suffering from BN, who are poorly identified even in specialist areas, and a high proportion do not receive timely treatment.

- To conduct a longitudinal study investigating the impact of AN on education, employment and potential earnings differential. It will also be helpful to gather longer-term follow-ups of clinical trials with accompanying economic evaluation to better reflect the longer-term costs of treatment and allowing us to estimate incidence-based costs of AN.

Acknowledgements

WP4: Activity and AN

WP5: Relapse prevention

WP6: Maternal ED

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Publications

WP 1a: Training school staff

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WP2a: Outpatient treatment

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WP2b: Inpatient treatment

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WP4: Activity and AN

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WP5: Relapse prevention

Peer-reviewed publications

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WP6: Maternal ED

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Appendices

Appendix 1: Training school teachers (WP1a)

Appendix 1.1: Student questionnaire

1. People who with eating disorders can be very good at hiding their problems - do you think you would know enough to tell whether a friend was at risk?
    a. Yes - I have spotted the signs in the past
    b. Yes - I am confident I would know what I'm looking for
    c. I'm unsure
    d. No - I think it's unlikely I would see the early signs
    e. Other (free text)

2. Has your school ever taught you about eating disorders, and what to do if you're worried about yourself or a friend?
    a. Yes, I have been taught and it was helpful
    b. Yes, I have been taught but it was NOT very helpful
    c. No, I have never been taught at school
    d. I can't remember
    e. Other (free text)

3. Can you think of anything your school could do to help you understand as much as you'd like to about eating disorders and how to help your friends if they're in difficulty? (free text)

4. If you were worried that a friend might have an eating disorder what would you do?
    a. My friend would probably talk to me, and I would listen and try to help
    b. I would approach my friend and raise the issue and we would work out together what to do
    c. I would talk to a teacher I trusted and ask for advice
    d. I would anonymously let a teacher know so they could help my friend, but my friend wouldn't know I had told on them
    e. I would talk to an adult outside of school (e.g. my parents or youth group worker)
    f. I wouldn't do anything at first, I would wait and see if things got worse or better
    g. Other (free text)

5. If you told a teacher that you were concerned about a friend, what would you <u>want</u> them to do?
    a. Talk to my friend and find out what was wrong
    b. Help me to help my friend
    c. Tell my friend's parents and get them to help
    d. Make sure my friend got support from a counsellor or doctor
    e. Nothing, just listen
    f. Other (free text)

6. If you told a teacher that you were concerned about a friend, what do you think they would <u>actually</u> do?
    a. Talk to my friend and find out what was wrong
    b. Help me to help my friend
    c. Tell my friend's parents and get them to help
    d. Make sure my friend got support from a counsellor or doctor
    e. Nothing, just listen
    f. Other (free text)

7. If you felt you should tell a teacher about a friend you were worried about - how would you most like to do it (even if it's not possible at the moment)?
    a. Face to face
    b. On the phone
    c. Text / SMS
    d. Email
    e. Instant messaging
    f. In writing
    g. Other (free text)

8. If you were suffering from an eating disorder - do you think your school would feel like a safe and supportive place to recover?
    a. Strongly Agree
    b. Agree
    c. Neutral
    d. Disagree
    e. Strongly Disagree

      f.   Other (free text)

9. Can you think of anything that would make your school an even better place for people recovering from an eating disorder? (free text)

10. Has your school ever helped you, or a friend, when you've needed help with regards to an eating disorder? (please explain) (free text)

11. Has your school ever failed to help / not noticed / made the situation worse when you or a friend needed help with regards to an eating disorder? (please explain) (free text)

Appendix 1.2: Staff questionnaire

1. Does your school / college have an eating disorders policy in place?
   a. Yes we have specific policies relating to eating disorders
   b. Yes - eating disorders are covered in another policy (e.g. child protection)
   c. Unsure
   d. No we definitely do not refer to eating disorders in any of our policies
   e. Any Further Comments(free text)

2. Do you think that policies that refer to eating disorders are effective? (only asked if answered yes to question 1)
   a. Very Effective
   b. Effective
   c. Ineffective
   d. Very Ineffective

3. Has your school offered any form of training / briefing about eating disorders?
   a. Yes
   b. No

4. Who attended the training? (only asked if answered yes to question 3)
   a. Just me
   b. All Pastoral Staff
   c. All Middle and Senior Managers
   d. Whole Staff
   e. NA
   f. Other (free text)

5. How was the training delivered? (only asked if answered yes to question 3)
   a. Written materials
   b. Face to face - workshop or seminar
   c. Face to face – lecture
   d. Over the Internet
   e. Over the phone
   f. NA

g. Other (free text)

6. What did you find useful about the training? (free text) (only asked if answered yes to question 3)

7. What would have made the training more useful? (free text) (only asked if answered yes to question 3)

8. If you have not received any training on eating disorders. Do you think you would find some training useful? (only asked if answered no to question 3)
    a. Yes - Very Useful
    b. Yes - Quite Useful
    c. No - Not Very Useful
    d. No - Not at all Useful
    e. Any Further Comments (free text)

9. Are you aware of any current or past cases of eating disorders in your school / college?
    a. Yes, I have been directly involved with cases
    b. Yes, I have been aware but not involved with any cases
    c. No, I have not been aware of any cases
    d. No, there have been no cases
    e. Any Further Comments (free text)

10. What would you do if you were concerned that a student may be suffering from an eating disorder? (free text)

11. In your school / college; if a student is concerned that one of their peers may have an eating disorder- what are they encouraged to do?
    a. All concerns are passed on to a specific member of staff
    b. The student could talk to any member of staff
    c. We have a texting / emailing / post-box service that students can anonymously use
    d. This is not something we have discussed with students
    e. Other (free text)

12. Have you had any particularly positive or negative experiences when communicating with parents regarding eating concerns? If so please briefly outline: (free text)

13. Have you worked with any outside agencies to support students with eating disorders? Please outline which agencies you have used and any particularly positive or negative experiences you have had. (free text)

14. Has your school / college ever had to re-integrate a student following a period away from school caused by an eating disorder?
    a. Yes
    b. No

15. Did staff or students receive any advice on how to best support the returning student? (only asked if answered yes to question 14)
    a. Yes
    b. No

16. Can you think of any further support that could have been given to staff or students that would have helped the returning student to reintegrate more successfully? (please outline) (free text)

17. When we develop our training materials for schools, we want to make sure they are as useful as possible. In order to do this, instead of inventing examples, we are collecting anonymous case studies from school staff which will be used for training purposes. If you have can think of any instances surrounding students, staff and/ or parents when dealing with eating disorders it would be helpful if you could provide a brief outline below: (free text)

Appendix 1.3: Eating disorders attitudes and knowledge questionnaire

My overall knowledge about eating disorders:

No knowledge   Full knowledge

1   2   3   4   5   6   7   8   9   10

My knowledge about the risk factors and causes of eating disorders

No knowledge   Full knowledge

1   2   3   4   5   6   7   8   9   10

My confidence in my ability to recognise the warning signs of an eating disorder in one of my students.

Not   at   all   Completely
confident   confident

1   2   3   4   5   6   7   8   9   10

My knowledge about the symptoms seen in eating disorders

No knowledge   Full knowledge

1   2   3   4   5   6   7   8   9   10

My knowledge about how to support a student with an eating disorder

No knowledge   Full knowledge

1   2   3   4   5   6   7   8   9   10

My confidence in my ability to support a student with an eating disorder

Not   at   all   Completely
confident   confident

1   2   3   4   5   6   7   8   9   10

My confidence in my ability to work with the parent/carer of a student with an eating disorder

Not   at   all   Completely
confident   confident

1   2   3   4   5   6   7   8   9   10

How confident would you feel teaching a lesson exploring student knowledge and attitudes about eating disorders?

Not   at   all   Completely
confident   confident

1   2   3   4   5   6   7   8   9   10

Please indicate how much you agree/disagree with the following statements about students with eating disorders.

With Reference to students with eating disorders	Strongly disagree	Disagree	Agree	Strongly agree
Symptoms of eating disorders are fairly common and will resolve over time without treatment				
Eating disorders are severe mental illnesses				
Students with eating disorders are to blame for their own condition				
Eating disorders have major consequences on the sufferer's quality of life				
Students with eating disorders cause difficulties for school staff				
Students with eating disorders cause difficulties for their peers				
Teaching students about eating disorders will make them more likely to develop one				
School staff should be involved in the treatment and recovery process for students with eating disorders				
Sufferers should not continue to attend school where other students may copy their behaviour				

School staff should review their academic expectations of students with eating disorders				
The school has a responsibility to support students suffering from eating disorders				
There is a lot the school can do to help during the recovery process				

Each of the following case studies is a real situation that has been outlined by a member of school staff in the past. As such, there are no right or wrong answers – but please answer the questions following each case study as honestly as possible.

> 12-year-old Zeena is a model student. She works very hard at everything she does and excels academically. She is usually top of the class and is disappointed even to come second. She always submits her homework on time and it is clear that she dedicates a lot of time to her studies at home as well as at school.
>
> Zeena has recently been fasting for Ramadan and decided to show her dedication to her faith by fasting beyond Ramadan. She has had her parents full support on this – they are very proud of Zeena's dedication to her faith. In fact, her parents play a huge role in her life, they are very encouraging of her academic achievements too and always encourage her to achieve to her very best and believe that she can achieve anything she wants to if she works hard enough.
>
> Zeena is well liked by her classmates though she seems a little more withdrawn in class than usual and has taken to spending many of her lunchtimes in the library alone. Although she is only in year 8, she has ambitions to study veterinary science and she understands from her parents and older brother that in order to realise her goal she must work very hard.

How confident would you feel in dealing with this situation?

15-year-old Simon is not a natural sportsman, but this year he has been putting his all into the football team. He has been attending every practice and keeping his fitness up by frequently visiting the gym between practices.

The slightly chubby looks that earned him the nickname 'Podge' in Year 9 are a thing of the past and instead Simon is building up quite a six-pack. He's even beginning to get some rather giggly attention from the girls – though he doesn't seem interested at all, preferring to shy away from the attention and work out in the gym during his lunch breaks and after school.

Simon lives with his younger brother and his mum who has been a single parent to both boys for as long as you have known them. She is very supportive of Simon and his brother but isn't always able to attend parents evenings as she works long hours to support the family.

How confident would you feel in dealing with this situation?

Not   at   all   Completely
confident   confident

1   2   3   4   5   6   7   8   9   10

16-year-old Karly is in your tutor group. She has recently been absent from school for half a term receiving treatment for Bulimia. She is due to start back at school soon. Whilst her condition is much improved and her physical health no longer in immediate danger, it has been made clear to you that Karly will require quite significant support to ensure she does not relapse. She is still in the process of recovery and will be for quite some time but her doctors and parents have agreed that with an appropriately supportive environment, it would be beneficial for her to

continue her recovery in school. She's a few months away from sitting her GCSEs and has several good friends at school though they have not seen much of her during her absence.

How confident would you feel in dealing with this situation?

Not at all   Completely
confident   confident

1   2   3   4   5   6   7   8   9   10

Appendix 2.1: Detailed results from qualitative evaluation

Main category	Generic category	Sub category	Frequency	Example
What have you learnt about yourself from this therapy?	Things I have learnt about myself	Bottle up emotions	8	"How I deal with emotions - that I bottle them up until they explode…"
		Block/avoid my emotions	6	"How I used to block my emotions and not be able to sit with them…"
		It's ok to express your feelings	6	"It's ok to talk about your problems, it makes you feel better afterwards."
		Not getting needs met	5	"…run into difficulties when I don't look after own needs."
		Good at caring for others	5	"I have also learnt that I am a great friend to others but not a great friend to myself."
	Skills I have begun using	Expressing/communicating more	7	"…better at being able to express feelings – more open in communicating positive and negatives."
		Positive intentions of negative emotions	6	"Negative feelings aren't always bad – they teach/protect…"

Main category	Generic category	Sub category	Frequency	Example
		Identifying emotions	5	"How to name emotions and how to find the right words for how I'm feeling."
		Look at the bigger picture	4	"….it's alright not to worry about the little details being perfect and to look at the bigger picture."
		Emotions are fluid	4	"…that emotions are fluid and change throughout the day."
		Other people's perspectives	3	"Being more aware of other people's perspectives"
		Acknowledging/accepting emotions	3	"…it is ok and acceptable to feel sad at times."
	Skills I would like to use	Be more assertive	3	"Need to be assertive"
		Be more open	3	"That I need to focus on communicating my emotions to those around me…."
		Be more positive	3	"I would like to be more positive. Being more pro-active can make positive things happen."
Were there any aspects which were particularly helpful?	Emotional strategies learnt	Labelling	5	"Looking more specifically at different emotions (e.g. labelling)."
		Acting before emotions spiral	4	"Also for me looking at ways to reduce emotions getting to that extreme point by acting on feelings before they start to spiral out of control"

Main category	Generic category	Sub category	Frequency	Example
		Communicating feelings	3	"…talking about your problems can actually help you deal with them."
		Non-specific strategies	3	"Strategies to manage difficult situations that occurred during the week."
		Recognising the positive intentions of emotions	3	"Looking at emotions in a different way e.g. positive meanings of negative emotions."
	Learning about emotions	Relation to needs	7	"The idea that each and every emotion is simply an indicator that I need something, or a guide to determine how I behave"
		Awareness of own difficulties	5	"…being more aware of the issues and difficulties that need attending to"
		Fluidity of emotions	4	"Knowing there are different emotions that we feel, it is ok to have other emotions rather than just feeling the same all the time."
	Aspects of the approach	Reflection time	6	"Having time/space to reflect on emotions and what they actually mean to me in everyday life."
		Doing homework	5	"Homework allows time to come up with good examples/reflect more."
		Empathy of therapist	4	"I was met with a very caring and compassionate

Main category	Generic category	Sub category	Frequency	Example
				approach and someone listening to how it was for me."
		Structure/ themes	3	"Structure/having themes to each session"
	All sessions were helpful	n/a	6	"To be honest every session has been beneficial…"
Were there any aspects that were particularly unhelpful?	Aspects of the approach	Initially too basic	3	"First few sessions seemed a little basic"
		Not personalised	2	"Tasks [were] statistic based rather than personal based."
		Too structured	1	"Sometimes too structured"
		Ended too quickly	1	"….it came to an end too quickly."
	Certain tasks/ sessions	Facial expressions	4	"Didn't gain a lot from the facial expressions exercises"
		CRT sessions	2	"Not sure at first - thinking about thinking"
		Physical manifestations	2	"Not helpful looking at how emotions feel in the body"
		Emotion switching	1	"Didn't take that much from emption switching session - already aware of switching emotions."
	No aspects	n/a	10	"None - learned something from everything"

Main category	Generic category	Sub category	Frequency	Example
	unhelpful			
What could be improved?	More sessions	Longer therapy	8	"The therapy here is the best I've encountered, the only criticism is there isn't more of it"
		Follow up sessions	1	"…a follow up course of CREST would be highly beneficial"
	Tailored more to individual	More in depth	4	"Taking the therapy to a more in depth level, relating emotions to an underlying thinking and beliefs and working from that level."
		More personalised	2	"If it was personalised, tailored to me/individual rather than generic to all."
	More on certain topics	Managing emotions	2	"More strategies – what to do in emotional situations."
		Emotions and needs	2	"More about emotions and their relationship to needs"
	Less on certain topics	Facial Expression	2	"A few less introductory sessions e.g. looking at faces"
	Nothing could be improved	n/a	4	"Nothing. I found the number of sessions to be just right and the length of sessions appropriate."
What strategies have	Having	Benefits of emotions	6	"Negative emotions can have a positive effect as

Main category	Generic category	Sub category	Frequency	Example
you learnt to use in the future?	emotional awareness			they can alert me to the fact that something needs to change and inspire me to take positive action"
		Bottling up is not helpful	4	"Remembering bottling up doesn't get me anywhere apart from frustrated and angry"
	Practical Skills	Talking/Communicating	17	"…expressing emotions in relation to difficult situations - voice what I am thinking or feeling."
		Being more assertive	9	"Being more assertive by speaking up more when needed"
		Having a positive attitude	7	"Focusing on positive things – reflecting on positives and being pro-active at making positive things happen"
		Labelling	6	"Able to identify feelings more accurately"
		Getting needs met	6	"Asking for help when I need it"
		Acknowledging emotions	6	Acknowledging how I feel
		Looking at the bigger picture	5	"I have learnt to look at the bigger picture when I am feeling anxious or worried about a certain situation"

Appendix 3: Economic analyses (WP7b)

Appendix 3.1: Data availability and assumptions for service-level cost analysis

The service-level data available to the economic evaluation included

- Level of service specialisation with regard to ED

- Service location (hospital or community)

- Details on ED assessment

    - Typical length of assessment

    - Staff typically involved in assessment

    - Outpatient treatment provided for AN

        o Type of treatments available

        o Typical length of session

        o Typical number of sessions

        o Staff typically providing the session

    - Details on other treatments provided, e.g. inpatient, day patient

The approximate cost of each type of treatment session was calculated by applying a set of assumptions:

- The unit costs for all staff members involved in the session were summed

- Where the questionnaire stated that one or another type of staff member provided the treatment (e.g. "psychiatrist or psychologist"), the average unit cost was used

- Where the typical length of treatment was missing, the length from a similar service (e.g. other non-specialist CAMHS) was applied

- For group treatments, a group size of six patients or families was assumed

Appendix 3.2: Individual-level analysis of treatment costs

The patient-level data provided the following information relevant to the economic analysis:

- Patient characteristics
- Patient clinical data (weight and height, Morgan-Russell criterion)
- Outpatient treatment:
    - Number of assessments
    - Number of individual or family sessions
    - Number of group, dietetic and medical outpatient sessions
    - Number and type of outpatient appointments for physical tests
    - Number of telephone consultations
    - Number of psychiatric reviews
- Number of inpatient days for ED or other reasons
- Services that had provided treatments or assessments

Appendix 3.3: Average costs of treatment by ED service type

	Specialist CEADS		Other ED services		Specialist CAMHS		Non-specialist CAMHS		Independent CEADS	
	Valid n	Mean £	Valid n	Mean £	Valid n	Mean £	Valid n	Mean £	Valid n	Mean £
Individual	3	£135	2	£124	6	£163	11	£163	3	£111
Group session	1	£32	2	£46	0	-	0	-	2	£78
IFT	3	£187	1	£258	5	£235	8	£246	2	£237
MFT day / session	1	£547	0	-	1	£547	1	£114	0	-
Parent session	1	£101	0	-	1	£22	1	£98	1	£120
Dietic session	3	£33	1	£62	3	£39	2	£109	2	£45
Occupational therapy	0	-	0	-	0	-	0	-	1	£36
Physiotherapy	0	-	0	-	0	-	0	-	1	£18

Appendix 3.4: Additional unit costs from publicly available sources

	£ per hour	Source	Notes
Doctors			
Associate specialist	166	PSSRU 2011, p. 202	time ratio as consultant (medical)
Consultant (assume medical)	202	PSSRU 2011, p. 203	time ratio from 2009 UC volume, 1.33
GP (hospital)	229	PSSRU 2011, p. 148	
GP (community)	138	PSSRU 2011, p. 148	
Paediatrician (hospital)	202	Medical consultant	
Paediatrician (community)	138	as GP	
Senior house officer	61	PSSRU 2011, p. 199 (foundation house officer year 2)	time ratio as consultant (medical)
Specialist registrar	89	based on PSSRU 2011, p. 201 (see notes doc for details)	time ratio as consultant (medical)
Staff doctor / ward doctor	117	based on medical consultant, check UC doc for details	time ratio as consultant (medical)
Nurses			
CAMHS nurse	75	based on CAMHS member schema with band 5 median salary	
CNS	73	PSSRU 2011, p. 142	community mental health nurse
Key nurse	120	PSSRU 2011, p. 192	
Nurse (hospital)	104	PSSRU 2011, p. 193	
Nurse (community)	71	PSSRU 2011, p. 141	
Psychology nurse	104	as specialist nurse	

Senior staff nurse	120	PSSRU 2011, p. 192	
Specialist nurse	104	PSSRU 2011, p. 193	
Specialist nurse (community)	89	based on PSSRU 2011, p. 144 nurse specialist	time ratio from RCN report
Psychologists & psychiatrists			
Child & adolescent psychiatrist	295	as generic psychiatrist	
Child psychiatrist	295	as generic psychiatrist	
Child psychiatrist (community)	293	as psychiatrists, overheads from CAMHS team	
Child psychologist (hospital)	156	as clinical psychologist, overheads as psychiatrist	
Child psychologist (community)	152	as clinical psychologist	
Clinical psychologist (hospital)	156	as clinical psychologist, overheads as psychiatrist	
Clinical psychologist (community)	152	PSSRU 2011, p. 137	face to face contact
Consultant psychiatrist (hospital	295	PSSRU 2011, p. 205	per hour patient-related
Psychiatrist (community)	293	as psychiatrists, overheads from CAMHS team	
Psychologist (hospital	156	as clinical psychologist, overheads as psychiatrist	
Psychologist (community)	152	as clinical psychologist	
psychology assistant	123	as clinical psychologist, median salary grade 6	
Therapists			
Art therapist (hospital)	139	Clinical psychologist, AfC band 7	

Art therapist (community)	136	Clinical psychologist, AfC band 7
Child psychotherapist	156	as clinical psychologist
Cognitive analytical therapist	139	Clinical psychologist, AfC band 7
Counselling psychotherapist	156	as clinical psychologist
Drama therapist	139	as art therapist
Family therapist (community)	183	Clinical psychologist, AfC band 8b
Family therapist (hospital)	186	
Psychotherapist (hospital)	156	as clinical psychologist
Psychotherapist (community)	152	as clinical psychologist
Systemic psychotherapist	156	as clinical psychologist
Therapist	156	as clinical psychologist
Dieticians		
Dietician (hospital)	36	PSSRU 2011, p. 184
Dietician (community)	34	Based on UC volume (hospital), capital overheads from CAMHS teams
Paediatric dietician	47	As specialist dietician
Specialist dietician	47	based on UC volume (hospital), salary band 6 (median)
Other		
Behaviourist	156	as clinical psychologist
CAMHS professional (hospital)	101	See CAMHS professional (community)
CAMHS professional	98	PSSRU 2011, p. 175 (targeted)

(community)			
Occupational therapist (community)	35	PSSRU 2011, p. 134	no time ratio applied
Occupational therapist (hospital)	36	PSSRU 2011, p. 182	no time ratio applied
Occupational therapist assistant	31	based on OT; AfC band 4 (assistant practitioner)	no time ratio applied
Physiotherapist (community)	35	PSSRU 2011, p. 133	no time ratio applied
Physiotherapist (hospital)	37	PSSRU 2011, p. 181	no time ratio applied
Social worker (child)	146	PSSRU 2011, p. 157	
Therapeutic carer	104	as hospital nurse	

Appendix 3.5: Assumptions and data sources regarding societal costs of AN

Distribution of treatment*:* Around a third of AN cases are treated exclusively in primary care (358). Based on HES, we estimate that around 11% of cases are treated as inpatients each year. This suggests that 56% are treated primarily on an outpatient basis.

Inpatient and outpatient treatment: The number of inpatient admissions, number of bed days and outpatient contacts recorded under a primary diagnosis of AN were obtained from the Hospital Episode Statistic for 2010/11 (408) and the Special Interest Topic on ED for the same year (396). Since a detailed breakdown by age was not available, the ratio of adult (63%) to child (37%) of Finished Consultant Episodes from the Special Interest Topic report was applied when costing inpatient stays. This served as a lower-bound estimate for inpatient costs because admissions that are causally related to AN may not be recorded under a primary diagnosis of AN, such as cardiac problems. To obtain a higher bound estimate, we applied the ratio of costs for medical inpatient admissions to ED admissions from the Care Pathways Study (see Section 2 above). For our higher estimate, we also included potential additional outpatient care costs, based on the ratio of the costs of ED-related and medical outpatient appointments to ED inpatient costs from the Care Pathways study, across all three pathways (38% and 27%, respectively). This includes treatment provided in community settings. Our provisional analysis of data relating to patients treated in the private sector indicates that outpatient treatment makes up a much smaller proportion of costs than in the public sector. We therefore apply this additional cost only to NHS beds (51% of ED inpatient costs).

Cost of independent sector provision: We identify the likely cost to the NHS of inpatient treatment provided by the independent sector, and additional costs of privately funded treatment based on the assumption that 49% of ED beds are provided by the private sector (379), and 90% of independent beds are NHS funded (31).

Primary care costs: Our lower estimate of primary care costs draws on estimates from the ProBono Economics report, where it was assumed that each person with AN saw their GP three times per year (70). Little is known about the service use of people with AN prior to entering treatment, but there is some evidence on elevated service use up to five years prior to diagnosis (21, 22). For our higher cost estimate, we draw on baseline information from the three trials analysed in section 2 to estimate a plausible range of primary care costs (GP,

nurse, dietician) incurred prior to an inpatient admission or outpatient treatment. Where treatment is provided exclusively in primary care, we assume that each person is in contact with their GP three times per year (Nice 2004 ED guidance).

Benefit payments: The Department of Work and Pensions (DWP) provided data on social security benefit payments made to people because of an ED. There were on average 810 females claiming Employment Support Allowance (ESA) for ED per quarter, with an average weekly amount of £90.25. Incapacity Benefit (IB) or Severe Disability Allowance (*SD*A) was paid to 1,308 females each quarter, with a weighted average weekly amount of £56.04. As the statistic does not distinguish between different EDs, we assumed that the proportion of benefits paid to people with AN corresponded to the proportion of ED admissions for AN in HES (71%).

Years of Potential Life Lost: YPLL were calculated based on based a survival analysis by Harbottle and Birmingham (397). The study assumed a standardised mortality rate (SMR) of around 10. Based on a recent review (67), we assumed an SMR of around 5 and halved the number of life years lost to ensure a conservative estimate. We present the total annual number of YPLL due to AN, discounted using a 3.5% rate and based of a life expectancy for females at birth of 82.4 (409). This is a simplified approach allowing a rough estimate only. YPLL were valued at £30,000, the threshold commonly recommended by NICE for a healthy life year gained. Since it is unlikely that these additional years will be lived at full health, we applied the disability weight for depression (46% reduction, (410)) to the final figure. The results of our analysis are shown in Table 54, below.

Table 54: Years of Potential Life Lost

Age of onset (years)	Reduction in life expectancy (397)	Number of new cases per year	Life years lost per case (discounted at 3.5%)	Total life years lost
10-14	24.8	359	2.8	1,005
15-19	24.6	773	3.55	2,744
20-24	23.9	337	4.65	1,567
25-29	23.3	346	5.96	2,062
30-34	22.7	53	7.52	399
35-39	22.1	53	8.97	475
40-44	21.6	22	11.09	244
45-49S	Assume 21.6	22	13.6	299
Total				8,796